POSITIVELY AWARE
HIV TREATMENT, PREVENTION AND HEALTH FROM **TPAN**
MARCH+APRIL 2021

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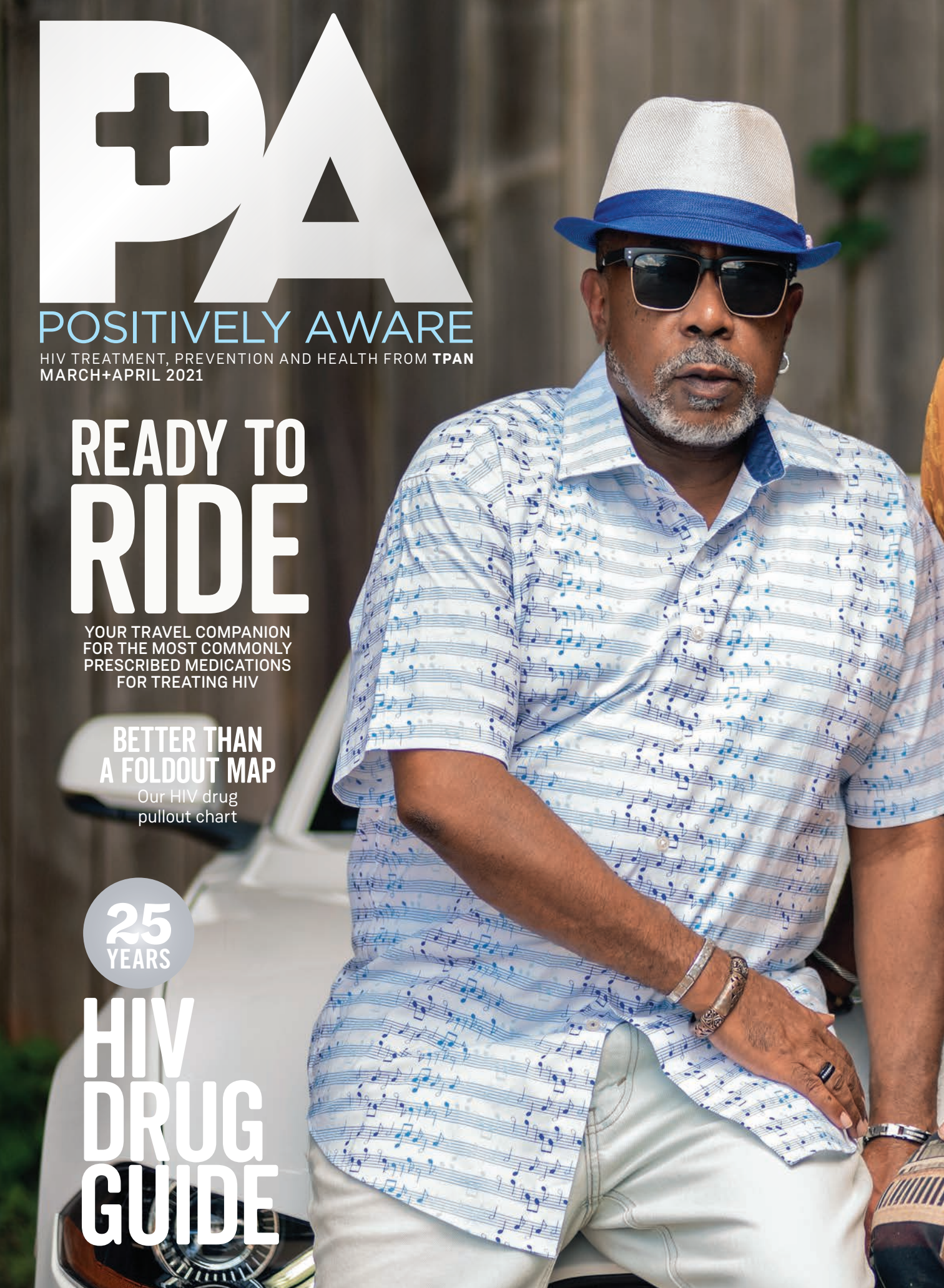
BETTER THAN A FOLDOUT MAP

Our HIV drug pullout chart

25 YEARS

HIV DRUG GUIDE



WATCH "HIV: It's Called Treatment as Prevention"

Learn about Treatment as Prevention (TasP) and see how staying on treatment can help protect you and the people you care about.

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STOPPING THE VIRUS CAN START WITH YOU.

Watch videos, share information, and see how we can all help stop the virus.

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GILEAD

START
HIV TREATMENT.

HELP PROTECT YOUR HEALTH.

There is no cure for HIV, but find out how treatment helps make it possible to live a healthier life.

SEE INSIDE





THE **PHARMACIST**

Eric K. Farmer, PharmD, BCPS, AAHIVP, is an HIV clinical pharmacist at the Indiana University Health LifeCare Clinic at Methodist Hospital in Indianapolis, one of the largest providers of HIV medical services in the state of Indiana. He 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 is on the Board of Directors for the American Academy of HIV Medicine and serves as clinical faculty for the Midwest AIDS Training and Education Center. 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 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**

Melanie Thompson, MD's career of over three decades has focused on ending the HIV pandemic, including conducting clinical research for HIV treatment and prevention, advising on HIV policy at the local and national level, developing national and international HIV treatment and care guidelines, and providing medical care for people with HIV. Between 1988 and 2020, she conducted over 400 studies in the areas of HIV treatment, prevention and diagnostics; viral hepatitis treatment and diagnostics; and sexually transmitted infection diagnostics as Principal Investigator of the AIDS Research Consortium of Atlanta (ARCA). She saw her first patient with HIV in 1982 and has cared for thousands of people with HIV in Atlanta since that time.

She currently co-chairs the HIV Medicine Association (HIVMA) HIV Primary Care Guidance Panel that recently published its 2020 recommendations for the clinical care of people with HIV in *Clinical Infectious Diseases* in November.

Dr. Thompson's passion is to contribute to an end to the HIV epidemic through patient-centered medical care, prevention and treatment research, and evidence-based guidelines and policy with a focus on health inequities.

THE **ACTIVIST**

Bridgette Picou is a licensed vocational nurse currently working in both the HIV and home health fronts. She helps student nurses understand the importance of compassionate and informed care to the health and mental well-being of people living a positive life. With an emphasis on women's voices and needs, her goal is to be a light for everyone struggling with HIV and navigating a new life process after diagnosis. Focusing on blogging, educating, and speaking at various conferences, Bridgette hopes that by normalizing the image of what HIV looks like, the stigma and fear can be reduced or eliminated. Quality of life is important to her as well as the idea of thriving rather than just surviving.

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 much a 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 over a decade. She works directly with patients focusing on adherence to HIV medication, managing other chronic diseases, and analyzing HIV medication resistance. Dr. Blieden has been working closely with City of Los Angeles officials and the Los Angeles Fire Department on deployment of the influenza and COVID vaccinations. Dr. Blieden is Assistant Professor of Clinical Pharmacy and Director of Student Outreach and Community Health at the USC School of Pharmacy. She reviewed the DHHS guidelines for this guide.

FARMER AND VÁZQUEZ: JOHN GRESS · BLIEDEN: ISAAC MORA · PHOTO COURTESY OF BRIDGETTE PICOU

Embrace the journey

BY **RICK GUASCO**

It started with a Ford Mustang convertible that Nathan Townsend had rented for the weekend to celebrate his birthday. The theme for the 25th annual POSITIVELY AWARE HIV Drug Guide was *Road Trip*, and the timing couldn't have been better for the cover photo shoot.

Life is often described as a journey. A road trip is a journey, not unlike living with HIV. You can be as prepared as possible—road map (or map app) in hand, your route charted, suitcase packed, gas tank topped off—but a road trip is often about encountering the unexpected. The sudden flat tire, getting lost—and loss of signal, discovering new sights, sharing new experiences, and meeting new people along the way.

TOWNSEND, 67, was diagnosed with HIV in October 1984. It was an unexpected turn.

"I went to get tested at a time when they said HIV was a white gay man's disease," he says. "It was purely a symbolic effort, or so I thought. I went to a community health clinic in Philadelphia with my partner of several years. When we got our results, his was negative and mine was positive. I really credit his response as the reason my response wasn't traumatic. He simply said, 'I guess we will have to start using condoms now.' So, I did not experience loss or rejection through diagnosis; I experienced love and acceptance."

As a witness to the AIDS epidemic of the 1980s and '90s, "the incredible wave of death in the '80s passed me by. I felt I had been spared, and because of that, I had to make it count. I found purpose in my pain.

"My sole job became making every moment count and living it to the fullest. Without an

CONTINUED ON PAGE 4 >>

NATHAN TOWNSEND

HABEEB MUKASA

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TPAN was founded in 1987 in Chicago as Test Positive Aware Network, when 17 individuals living with HIV 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.

BE GREEN.
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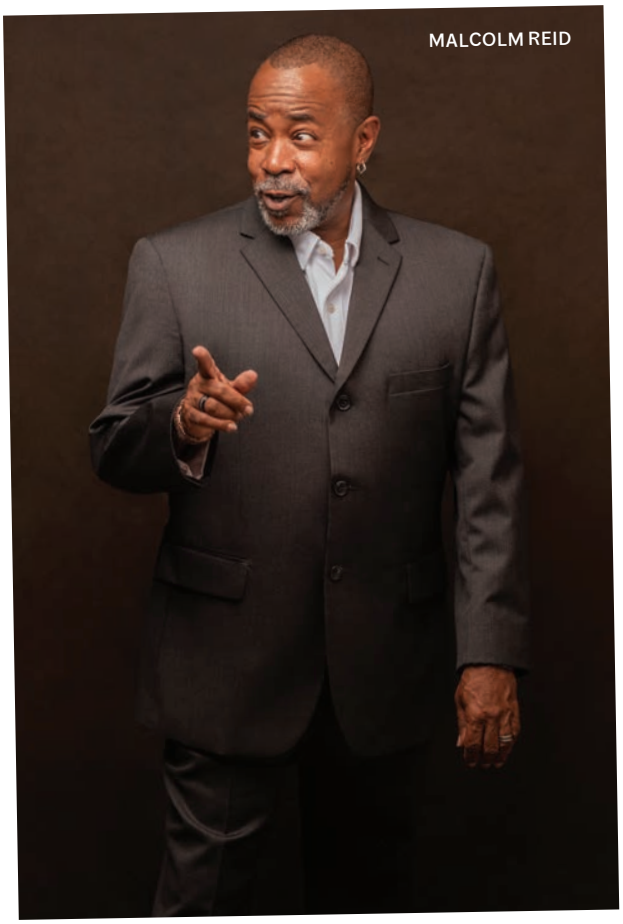
Embrace the journey

>> CONTINUED FROM PAGE 3

expectation of longevity, it became my fate to explore all that I could be, which led me to explore many opportunities, gifts, and talents. My entire life with HIV has been one of self-discovery and reinvention, and now almost 40 years later I'm still writing new chapters.

"The forks in the roads have been my life choices. Sometimes it appeared that I took a wrong turn, but ultimately it was the right choice to get the life lesson behind that choice."

Now an HIV advocate and mentor living in Atlanta, he is the administrator of a group home for people recovering from HIV-related hospital stays, a member of the local HIV Planning Council, and a care outreach specialist for a community clinic. He points to his faith as a source of strength and guidance. "HIV has made me fearless on a journey of hope and help. As the Bible says, '...let us not be weary in well doing; for in due season we shall reap, if we faint not.' This keeps me going; it keeps me grounded."


MALCOLM REID

FOR MALCOLM REID, 63, having tested positive 24 years ago, it's been a long road, winding through different landscapes. After decades working at a major telecommunications company, he began a second career in HIV advocacy, volunteering at THRIVE SS. The Atlanta-based community-based organization provides a variety of support services for Black gay and bisexual men living with HIV. Reid co-founded THRIVE's Silver Lining Project, which creates a safe virtual and physical space for older Black men living with HIV. Today, he is THRIVE's director of programs, which includes overseeing the Silver Lining Project.

"The engine of my life's journey is my sense of purpose," Reid says. "I work every day to make sure that our programing and advocacy are making a positive impact on people living with HIV, especially Black gay men, and those over 50, who face long-term stigma. Personally, I try to show a proud, happy thriving face and attitude, so that everyone in our network and everyone that we encounter, hear us when we say, 'you can live and THRIVE with HIV with no shame and no stigma. Live life abundantly.' This is a new career for me. After a long career in the corporate world, I enjoy learning new things and I'm not shy about trying new things. The culture we have built at THRIVE SS fosters a 'Let's Do, Can Do' attitude.

"My life's journey with HIV has been like a road trip with uphill climbs, downhill slides, some vicious curves, multiple stops in strange and wonderful places, but most of all, encounters with great people along the way, some of whom have become great friends.

"I started this road trip 24 years ago, and didn't think it was going to last this long," he says. "I thought the final destination was death, and while that is still true for all of us, that rocky, bumpy mountain road has been well paved. It's the autobahn, and I'm cruising in my convertible, top down, house music pumping, and dancing in my seat."

Reid and Townsend were photographed by Atlanta photographer **Habeeb Mukasa** (@habeebmukasa).

CORRECTION
Tivicay pediatric weight
A *Briefly* item in January + February ("Liquid Tivicay for Infants") gave an incorrect weight for pediatric dosing in the U.S. It should be "at least 6.6 pounds," not 77 pounds. POSITIVELY AWARE apologizes for the error.

HABEEB MUKASA

THE 25TH ANNUAL HIV DRUG GUIDE

MARCH+APRIL 2021

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EVERY ISSUE

IN THIS ISSUE

THE 25TH ANNUAL HIV DRUG GUIDE

A handbook of the medications used for treating HIV.
BY **ERIC K. FARMER, PharmD** AND **ENID VÁZQUEZ**
WITH COMMENTS BY **MELANIE THOMPSON, MD** AND **BRIDGETTE PICOU**

20–61

'The engine of my life's journey is my sense of purpose.'
—Malcolm Reid, PAGE 4

THE CATEGORY IS...

ROAD TRIP REALNESS

What's been the most unexpected experience or encounter you've had in your journey with HIV?

That's the question we asked our followers on Facebook, Instagram, and Twitter. They served up some honest feelings and experiences

"I was diagnosed in January of '92. I was 32 years old, and had never met a gay person, but it was the gay community in my 12 Step groups that guided me, supported me, sat on the phone for hours listening to me cry because I refused to burden my children with more of my issues. They were the ones who showed me which doctors were best, who got me a job—the list goes on and on. I grew up in a Baptist home, and although I had always questioned the misogyny and why we only send 'thoughts and prayers' to folks in need instead of actually doing something, homosexuality was never talked about out loud—hell, we never discussed any real life issues—so, the fact that the heterosexual community exiled me put many things into perspective."

—ROSE McCLOUD

"The most unexpected thing I have encountered thus far on my 25-plus year journey with HIV, is simply that it is okay to be living with HIV. Living with HIV has provided me with courage and strength to advocate for and help others living with HIV. I have become a better version of myself because of my long journey with HIV. All of this has been extraordinary, because I never thought I would be a long-term survivor. Simply, it is okay for me to be living with HIV, an unexpected gift that has enabled me to dream, to live, and to embrace love!"

—JASAN M. WARD

"Becoming 'accidental advocates' in the community has been the biggest unexpected thing that has happened in our 36 years of marriage and on our 14-year journey following our HIV diagnosis. As a couple, we were really laid back and quiet. After our diagnosis we fought to survive in a community where we didn't see many people like us, we were actually accepted by the gay community. So, we stepped out to create a space where we could reach out to those in need to make a difference. The promise we made to each other after our diagnoses was to reach out and pull others up who need a hand. We developed a stronger bond between us as we worked together in the HIV community.

—EUNICE AND KALVIN MARSHALL

"The most unexpected part of my HIV diagnosis and living with HIV for nearly half my life now is the strength it's given me. Though it hasn't been easy, overcoming what was a death sentence can be very empowering.

— JEFFERY PARKS

"The ignorance of trained medical professionals. In 2000, I was pregnant, and was advised to consider termination by my OB. My daughter is HV negative, healthy and beautiful! In 2010, I told a dentist hygienist I had HIV, and she returned to do my dental cleaning in a full hazmat suit. The office didn't routinely wear face shields. I "schooled" their office manager. In 2019, the podiatrist doing my foot surgery informed me he would alert OR staff I had HIV so they could take extra precautions. I countered that all medical professionals are supposed to take universal precautions. Other than people specialized in HIV care, the ignorance in the medical field is astounding even 27 years into my HIV journey!"

—XIO MORA-LOPEZ

"For me, it's been unpacking internalized HIV stigma. One would think that living my life openly about being HIV positive, that this wouldn't be an issue, but I find it popping up at the oddest of times and situations. I've also had a hard time with AIDS organizations and community-based organizations that say "we need more involvement of people living with HIV," but when we do get involved and push back on fear mongering messaging, or that services aren't equitable, that we are labeled as problematic and told that's not the kind of involvement they wanted.

—BRADY DALE ETZKORN-MORRIS

"For me, it has been the unwillingness of myself to be myself. Also, the constant struggle with the local AIDS service organization; in one breath they say that they want input from people living with HIV and from long-term survivors, but in the next breath, they seem to say they only want want to hear what they want to hear. There are a few "powers that be" at the local ASO that talk to talk; they don't listen. They tell us what we need, instead of listening to what we need or want.

—MARK L GRANTHAM

JOIN IN THE CONVERSATION

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EDITOR'S NOTE

JEFF BERRY
@PAeditor

Silver Edition

This issue of POSITIVELY AWARE magazine is our 25th Annual HIV Drug Guide, and it's been quite a ride. We've come a long way since that first drug guide in 1997, which had nine antiretrovirals listed in it, most of which had pretty severe side effects and tolerability issues; only a few are prescribed anymore. It was 15 years before that, in 1981, when the first cases of Kaposi sarcoma among five gay men in Los Angeles were reported in the CDC's *Morbidity and Mortality Weekly Report* (*MMWR*). It was one of many opportunistic infections that would be associated with the virus that would later come to be known as HIV, the cause of AIDS.

1997 was around the same time that the first protease inhibitors came to market, followed by combination therapy (using several drugs from different drug classes to target the virus), both of which ultimately changed the trajectory of the HIV pandemic. It took a full 15 years or more to finally start to have effective treatments that are tolerable, and to begin to find hope again—but HIV is still with us after 40 years, and we don't yet have an HIV vaccine (more on that later).

What many of us do have, thankfully (because we have survived), is the ability to look back with the perspective that one day we will eventually have effective treatments for COVID-19 as well. But SARS-COV-2 (the virus that causes COVID-19) is probably here to stay, at least for the time being. Just as we learned to adjust our behavior at the height of the HIV pandemic by limiting our partners, using protection for sex and clean needles when injecting drugs, we're learning to adjust again by wearing masks, physical distancing, and washing our hands frequently. It won't be forever (well, maybe the washing hands part will), but it may take some time—years in fact—to get to our new normal, so we have to be prepared for the long haul. We did it before, and we can do it again. We just have to remain hopeful, and do our part.

Part of doing your part is getting vaccinated if your health allows, and when it's your turn. There are differing schools of thought on whether or not people living with HIV should move to the front of the line—if your immune system is severely compromised, or you can't get to viral suppression, it's probably a good idea. In a few months there will hopefully be enough vaccine and distribution centers to get most people in the U.S. who are eligible vaccinated by the end of the summer. But we still need to make sure that vaccine education and awareness is reaching people of color and marginalized populations that are disproportionately affected by COVID-19, and that vaccines are getting distributed equitably and available in the communities where they are most needed.

The speed with which vaccines were developed in the last year has been nothing short of remarkable, so why don't we have an HIV vaccine? Well, it's just a very different virus. HIV is designed to evade our immune system, while the COVID virus is relatively easy to vaccinate against—the antibodies our immune system develops when we get the vaccine are quite effective at protecting a person.

Nonetheless, the death toll from COVID has been staggering, just as the death toll from HIV and AIDS has been, and continues to be. If there is any silver lining in this our silver anniversary issue, it is that we have reason to be hopeful. Hope is what got us through some very dark times in the 1980s and '90s, and is what we have to hang on to now. It's been quite a ride, but I'm not ready for it to be over quite yet.

P.S. Thanks to all of the wonderful people who have made the POSITIVELY AWARE 25th Anniversary HIV Drug Guide possible, including Enid Vázquez, Rick Guasco, Eric Farmer, PharmD, Dr. Melanie Thompson, Carla Blieden, PharmD, Bridgette Picou, Jason Lancaster, and Habeeb Mukasa.

The speed with which vaccines were developed in the last year has been nothing short of remarkable, so why don't we have an HIV vaccine? Well, it's just a very different virus.

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What is SYMTUZA® Used For?

SYMTUZA® is a prescription medicine that is used without other antiretroviral medicines to treat Human Immunodeficiency Virus-1 (HIV-1) infection in adults and children who weigh at least 88 pounds (40 kg) who:

- have not received anti-HIV-1 medicines in the past, **or**
- when their healthcare provider determines that they meet certain requirements.

HIV-1 is the virus that causes AIDS (Acquired Immune Deficiency Syndrome). It is not known if SYMTUZA® is safe and effective in children weighing less than 88 pounds (40 kg).

Take SYMTUZA® exactly as your healthcare provider tells you. Do not change your dose or stop taking SYMTUZA® without talking to your healthcare provider. If you have difficulty swallowing, the tablet may be split using a tablet-cutter. After splitting the tablet, the entire dose (both halves) should then be taken right away. Do not miss a dose of SYMTUZA®. When your SYMTUZA® supply starts to run low, get more from your healthcare provider or pharmacy. This is very important because the amount of virus in your blood may increase if the medicine is stopped for even a short time. The virus may develop resistance to SYMTUZA® and become harder to treat.

What are the most serious risks with SYMTUZA®?

SYMTUZA® can cause serious side effects including: Worsening of hepatitis B virus (HBV) infection. Your healthcare provider will test you for HBV before starting treatment with SYMTUZA®. If you have HBV infection and take SYMTUZA®, your HBV may get worse (flare-up) if you stop taking SYMTUZA®. If you stop taking SYMTUZA®, your healthcare provider will need to check your health often and do blood tests regularly for several months to check your HBV infection or give you a medicine to treat your HBV infection. Tell your healthcare provider about any new or unusual symptoms you may have after you stop taking SYMTUZA®.

What are the important warnings?

- **SYMTUZA® may cause severe liver problems that can lead to death. Tell your healthcare provider right away if you get these symptoms:** skin or the white part of your eyes turns yellow, dark "tea-colored" urine, light-colored stools, loss of appetite for several days or longer, nausea, vomiting, or stomach area pain
- **SYMTUZA® may cause severe or life-threatening skin reactions or rashes. Stop taking SYMTUZA® and call your healthcare provider right away if you develop any skin changes with the following symptoms:** fever, tiredness, muscle or joint pain, blisters or skin lesions, mouth sores or ulcers, and/or red or inflamed eyes, like "pink eye" (conjunctivitis)
- **SYMTUZA® can cause new or worse kidney problems, including kidney failure**

What should I tell my healthcare provider?

Before taking SYMTUZA®, tell your healthcare provider about all of your medical conditions, including if you:

- have liver problems (including hepatitis B or hepatitis C)
- have kidney problems
- are allergic to sulfa (sulfonamide)
- have diabetes
- have hemophilia
- Are pregnant or plan to become pregnant. SYMTUZA® should not be used in pregnant women. It is not known if SYMTUZA® will harm your unborn baby
- Are breastfeeding or plan to breastfeed. You should not breastfeed if you have HIV-1 because of the risk of passing HIV to your baby.

  Do not breastfeed if you take SYMTUZA®.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Some medicines interact with SYMTUZA®. Keep a list of your medicines to show your healthcare provider and pharmacist. **Do not start taking a new medicine without telling your healthcare provider.**

Who should not take SYMTUZA®?

- Do not take SYMTUZA® with any of the following medicines: alfuzosin, carbamazepine, cisapride, colchicine (if you have liver or kidney problems), dronedarone, elbasvir and grazoprevir, ergot-containing medicines (such as: dihydroergotamine, ergotamine tartrate, methylergonovine), ivabradine, lomitapide, lovastatin or a product that contains lovastatin, lurasidone, midazolam (when taken by mouth), naloxegol, phenobarbital, phenytoin, pimozide, ranolazine, rifampin, sildenafil when used for pulmonary arterial hypertension (PAH), simvastatin or a product that contains simvastatin, St. John's wort (*Hypericum perforatum*) or a product that contains St. John's wort, or triazolam
- Serious problems can happen if you take any of these medicines with SYMTUZA®

What are the possible side effects of SYMTUZA®?

SYMTUZA® may cause serious side effects including:

- Immune system changes (Immune Reconstitution Syndrome) can happen in people taking HIV-1 medicines
- Too much lactic acid in your blood (lactic acidosis) which is a serious but rare medical emergency that can lead to death. **Tell your healthcare provider right away if you get these symptoms:** weakness or being more tired than usual, unusual muscle pain, being short of breath or fast breathing, stomach pain with nausea and vomiting, cold or blue hands and feet, feel dizzy or lightheaded, or a fast or abnormal heartbeat
- Diabetes and high blood sugar
- Changes in body fat can happen in people taking HIV-1 medications
- Increased bleeding in people with hemophilia, which can happen when taking protease inhibitors.

The most common side effects are:

- diarrhea, nausea, headache, gas, rash, fatigue, stomach problems

These are not all of the possible side effects of SYMTUZA®. Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

What important facts should I know?

This information is not complete. To get more information:

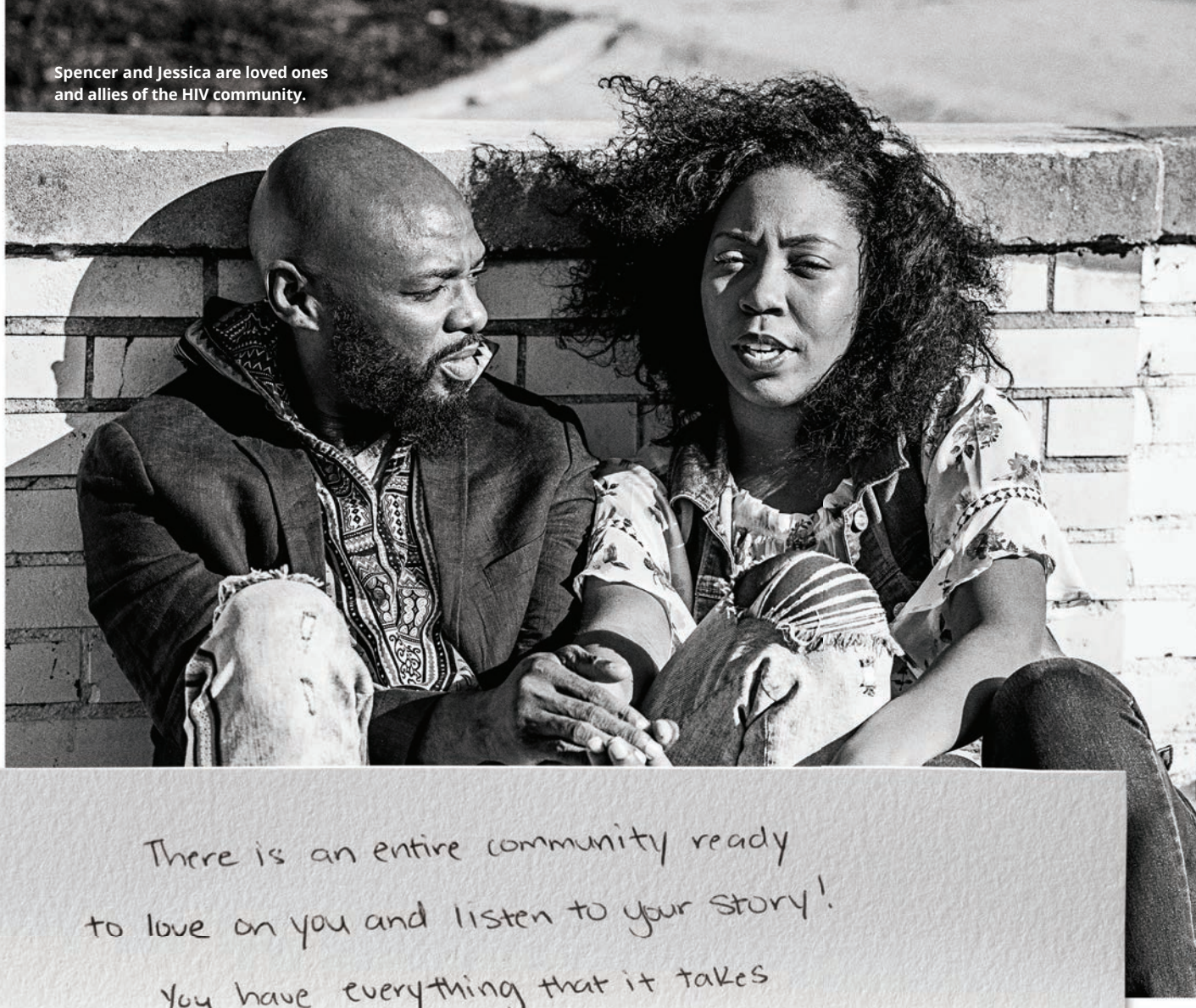
- Talk to your healthcare provider or pharmacist
- Visit www.SYMTUZA.com to read over the FDA-approved product labeling and patient information

cp-60855v6

Janssen Infectious Diseases

Please read above Important Brief Summary, including Important Warnings for SYMTUZA®, and discuss any questions you have with your doctor.

You may report side effects to the FDA at 1-800-FDA-1088 or to Janssen Products, LP at 1-800-JANSSEN (1-800-526-7736).



Spencer and Jessica are loved ones and allies of the HIV community.

Support Moves Us Forward

Moving forward is who we are, and when it comes to treating HIV, the only way forward is with support. Lean on friends, support groups, allies—and ask a healthcare provider how one-pill, once-daily SYMTUZA® may help you reach and stay undetectable* (<50 copies/mL).

*You must continuously take SYMTUZA® as prescribed.

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Self-defense moves

Take care of yourself in a time of stress

BY **BRIDGETTE PICOU**

I've never actually taken a self-defense class. The thought crossed my mind a few times as an adult, mostly when I heard stories of women who had been attacked or molested. In a way, I got self-defense lessons all through childhood. Older cousins and neighbors who wanted to make sure I could take care of myself poked, prodded, and harassed me until I got it right. Hands up, thumbs out, stick and move.

The thing is that over time, I came to realize that self-defense is not always a physical fight. It's not always a Bruce Lee-style beatdown. Sometimes—much of the time—it's more about mental agility than physical dexterity. Taking the power out of fear and putting it into hope. Learning to anticipate the danger or threat, and maneuvering out of the way. At the very least, adapt and change. Learn what you can about the threat, and let that guide you.

I don't know how else to put it, but the *everything-ness* of the past year made that more clear than ever. You can't very well punch racial injustice or drop kick a virus, right? I won't ever forget the early times of my HIV diagnosis when I was so frustrated and angry, I just wanted to hit something all the time. Later I recognized it was just fear of the unknown and insecurity. That's a different kind of self-defense though, right?

The ebb and flow of COVID-19 and the Black Lives Matter movement (the two things that hit me hardest) brought those feelings back and made my fight-or-flight adrenaline kick in with a vengeance. I tend to be a nurturer by nature, and while my instincts are generally to care and comfort, I definitely felt some of that stick-and-move energy. To be sure a confusing and stressful time, but I tried to remind myself to translate the old lessons into new strategies. Stick and move. Adapt.

As a nurse considered an essential worker, much of my routine didn't change, which has been a blessing. I am still taking care of others, but with the added weight of constantly being worried about exposure to COVID and then inadvertently exposing a more vulnerable patient, so this is a new fear I carry.

I live with HIV, and have had people physically recoil from me when they found out. Emotionally as well, which is just as bad if not worse. Even before that diagnosis I was *never* a person who wouldn't hug someone or touch them to give them comfort. COVID changed that. That stupid elbow bump greeting and social distancing go against all my instincts. I have never been a germaphobe, but I wash my hands a whole lot! This new "don't touch" thing? No hugging thing? It still takes getting used to. I'm actually sad that it's becoming easier to *not* touch people. That kind of worry turns to stress, and stress turns into anxiety. Self-defense for this was to remember to do the best I could. Wash my hands, clean the rooms between patients, and not expose myself unnecessarily.

I've had losses this year. I'm not alone. I would go out on a limb and say all of us have. Big, small, infinitely precious or mundane, we have all lost or had to give something up we weren't prepared to let go. I've watched people go from happy and open to shut down and in survival mode.

Let me encourage you to practice self-defense. Care for yourself. Don't forget that you matter. Get out into the sunlight. Polish your toes and buy the shoes. Take your medications and see your doctor. Do the little things that make you happy and that bring you moments of peace and joy. Give yourself, and those around you, the space and grace to grieve and adapt. Fight for people who can't fight for themselves. Find your joy and laugh. All of the things we forget to do sometimes when we are caught up in survival mode. Stick and move, friend. Stick and move.

Bridgette Picou wrote the activist comments for this year's HIV Drug Guide. She is a licensed vocational nurse in Palm Springs, California. She is also an active HIV blogger and contributor to the CDC's "Treatment Works" public service campaign. Finding a voice in advocacy and activism is a natural progression, since she feels that every time she fights for someone else, she affirms her own life.

OLGA STRELNIKOVA/ISTOCK

Choosing your route

DHHS Guidelines for people starting HIV therapy for the first time

The expert panel of the U.S. Department of Health and Human Services recommends starting antiretroviral therapy (ART) as soon as possible after HIV is diagnosed, regardless of CD4 count. Most people starting HIV treatment for the first time (treatment-naïve) should take one of the following: Biktarvy; Dovato; Triumeq; Tivicay plus Descovy or Truvada; or Isentress HD or Isentress with Descovy or Truvada. GO TO hivinfo.nih.gov for more information.

★ Recommended initial regimens for most people with HIV

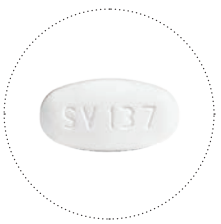
Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use.

INSTI + 2 NRTIs

Biktarvy
BIC / FTC / TAF
A1

Triumeq
DTG / ABC / 3TC
(if HLA-B*5701-negative)
A1

INSTI + 1 NRTI



Dovato
DTG / 3TC
A1

Except for individuals with pre-treatment HIV viral load greater than 500,000 copies/mL; who are known to have active hepatitis B virus (HBV) co-infection; or who will start ART before results of HIV genotype testing for reverse transcriptase or HBV testing are available

INSTI + 2 NRTIs

Tivicay
DTG

WITH

Descovy
FTC / TAF

OR

Truvada
FTC / TDF

A1

OR

Isentress HD (two tablets once daily)
or **Isentress** (1 tablet twice daily)
RAL

WITH

Descovy
FTC / TAF
B2

OR

Truvada
FTC / TDF
B1

RATING OF RECOMMENDATIONS
A: Strong B: Moderate C: Optional

RATING OF EVIDENCE
1: Data from randomized controlled trials. 2: 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. 3: Expert opinion.

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

Atripla: EFV/FTC/TDF **Biktarvy:** BIC/FTC/TAF **Cimduo or Temixys:** 3TC/TDF
Complera: RPV/FTC/TDF **Delstrigo:** DOR/3TC/TDF **Descovy:** FTC/TAF
Dovato: DTG/3TC **Epzicom:** ABC/3TC **Evotaz:** ATV/c
Genvoya: EVG/c/FTC/TAF **Odefsey:** RPV/FTC/TAF **Prezcobix:** DRV/c
Stribild: EVG/c/FTC/TDF **Symfi:** EFV 600 mg/3TC/TDF
Symfi Lo: EFV 400 mg/3TC/TDF **Symtuza:** DRV/c/FTC/TAF
Triumeq: DTG/ABC/3TC **Truvada:** FTC/TDF

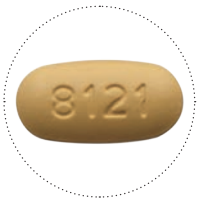
ISTOCK

✔ Recommended initial regimens in certain clinical situations

These regimens are effective and tolerable, but have some disadvantages when compared with the regimens listed on the previous page, 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.)



Symtuza
DRV / COBI / FTC / TAF
A1

Prezcobix
DRV / COBI

OR

Prezista
DRV 800 mg

Norvir
RTV

WITH

Descovy
FTC / TAF

OR

Truvada
FTC / TDF

A1

Evotaz
ATV / COBI

OR

Reyataz
ATV

Norvir
RTV

B1

WITH

Descovy
FTC / TAF

OR

Truvada
FTC / TDF

Prezcobix
DRV/ COBI

OR

Prezista
DRV 800 mg

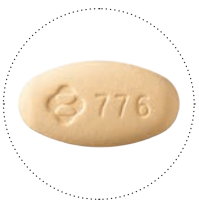
Norvir
RTV

B2

WITH

Epzicom
ABC / 3TC
if HLA-B*5701 negative

NNRTI + 2 NRTIs



Delstrigo
DOR / 3TC / TDF
B1

Pifeltro
DOR

WITH

Descovy
FTC / TAF

B3

✔ Recommended initial regimens in certain clinical situations (continued)

NNRTI + 2 NRTIs

3TC may substitute for FTC and vice v

Atripla
EFV 600 mg / FTC / TDF
B1

Symfi
EFV 600 mg / 3TC / TDF
B1

Symfi Lo
EFV 400 mg / 3TC / TDF
B1

Sustiva
EFV 600 mg

WITH

Descovy
FTC / TAF
B2

If viral load is less than 100,000 copies/mL and CD4 count is more than 200 cells/mm^3

Odefsey
RPV / FTC / TAF
B1

Complera
RPV / FTC / TDF
B1

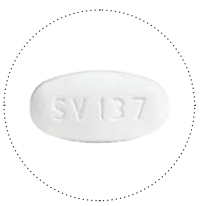
Boosted INSTI + 2 NRTIs

Genvoya
EVG / COBI / FTC / TAF
B1

Stribild
EVG / COBI / FTC / TDF
B1

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

Except for individuals with pre-treatment HIV viral load greater than 500,000 copies/mL; who are known to have active hepatitis B virus (HBV) coinfection; or who will start ART before results of HIV genotype testing for reverse transcriptase or HBV testing are available



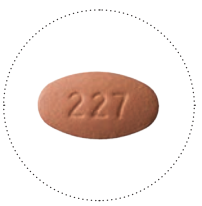
Dovato
DTG / 3TC
A1

Prezista
DRV 800 mg

+

Norvir
RTV

WITH



Isentress
(one tablet twice daily)
RAL

If viral load is less than 100,000 copies/mL and CD4 count is more than 200 cells/mm^3
C1

Prezista
DRV 800 mg

+

Norvir
RTV
C1

WITH

Epivir
3TC

12 things to know about HIV

1. When should HIV treatment start?
It is recommended that everyone living with HIV be on HIV treatment, and as soon as possible after diagnosis. So say the HIV treatment guidelines from the U.S. Department of Health and Human Services (DHHS).

2. What does HIV treatment do?
The goal of therapy is to suppress the amount of virus (called "viral load") 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. It also means you can't transmit HIV to your partner when you are on antiretroviral treatment (ART) and undetectable at less than 200 copies for at least six months (undetectable equal untransmittable, or U=U; also called "treatment as prevention," or TasP). HIV treatment should also raise the number of your CD4+ T cells, a measure of the immune system.

3. What tests are needed before taking HIV therapy?
You will be tested for STIs, hepatitis B and C virus, and HIV drug resistance. With the "Rapid Start" strategy recommended by DHHS, you will begin treatment while awaiting test results. Not all HIV meds are recommended for Rapid Start.

4. Is HIV treatment a cure?
Treatment does not cure HIV, but maintains health and prevents transmission.

5. What does HIV treatment consist of?
HIV therapy consists of medications from at least two drug classes. HIV drugs are called "antiretrovirals" (ARVs). To quickly find your drug, go to "Getting Around" in this issue. A single-tablet regimen (STR) consists of two or more ARVs which represent at least two drug classes and form a complete HIV treatment in one pill taken once daily. STRs are widely used by people taking HIV treatment for the first time (called "treatment naïve"), but they are

HABEEB MUKASA

treatment

not for everybody, including some people who are treatment-experienced or have multi-drug resistance. A fixed-dose combination (FDC) also combines two or more ARVs in one pill, but most consist of the same drug class and must be taken with at least one other HIV medication. An STR is a type of fixed-dose combination. This year sees the introduction of a long-acting injectable regimen (Cabenuva), which consists of two intramuscular injections taken every four weeks. See how the drugs work on page 18.

6. How should HIV treatment be taken?

Getting to and staying undetectable requires adherence: taking your medication as prescribed (for example, with or without food) and not missing doses. Discuss any concerns with your doctor, nurse, or pharmacist. Reach out for support—and continue to look for it. That includes housing and job opportunities if you need them! Anti-stigma efforts are also becoming more important for HIV care.

7. What is drug resistance?

If treatment is taken incorrectly, the virus might mutate (make changes in its viral genetic structure). This can make therapy less effective or even ineffective. This drug resistance occurs mostly through missed doses. Fortunately, many of the widely used HIV drugs today have a high barrier to resistance. However, it is better to avoid missing doses. Drug resistance may lead to the need for more complicated therapy (such as more pills or more drug classes).

8. Which drugs should I use?

HIV treatment is based on considerations such as health status (for example, kidney or liver disease) and lifestyle. See considerations for therapy in the DHHS guidelines.

9. How can I address my concerns?

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. While ARV regimens are usually well tolerated, each ARV can have side effects. Some may be serious. Refer to the drug page for each individual drug. Each person is different, and you and your health care provider will have to decide which drugs to use.

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.

10. What is AWP?

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. That's why it's commonly referred to as "ain't what's paid." In the drug cost-sharing and patient assistance program charts (beginning on page 65) we include information on how to access programs that can help cover all or part of the costs of these medications.

11. What are PEP and PrEP?

PEP and PrEP are not HIV treatment, but are HIV medications used by HIV-negative people to prevent infection with the virus. "PEP" stands for "post-exposure prophylaxis" and is taken for 28 days following a potential exposure to the virus. "PrEP" stands for "pre-exposure prophylaxis" and is taken daily to ward off HIV infection. "Prophylaxis" means "preventative."

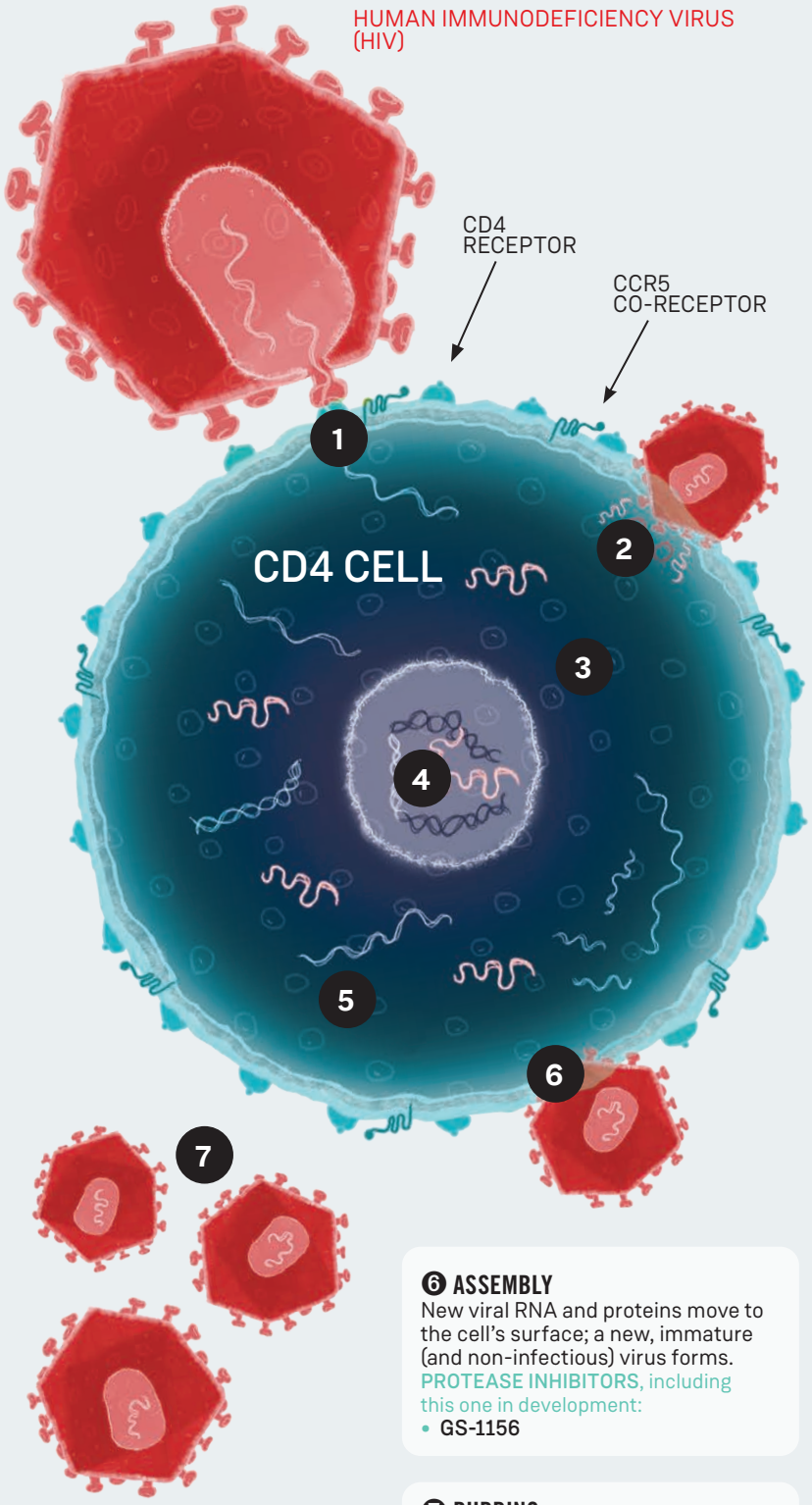
12. More information online

See considerations for therapy, including information on COVID, and drug factsheets from DHHS at HIVinfo.nih.gov. **DOWNLOAD** iPhone and Android apps that provide drug info, guidelines, and a glossary: clinicalinfo.hiv.gov/en. The International AIDS Society also produces HIV treatment guidelines. **GO TO** iasusa.org/resources/guidelines. To see if your HIV drug interacts with another medication, both prescription and over-the-counter, **GO TO** hiv-druginteractions.org. A good community-based source of information, besides POSITIVELY AWARE, is aidsmap.com.

HIV life cycle

Different drug classes interrupt the virus from replicating at various stages

ANTIRETROVIRAL THERAPY works by targeting more than one stage in the HIV life cycle. Combining certain drugs from more than one drug class will achieve this goal, and suppress the virus to undetectable levels in the blood. The compounds listed under the stages below are new drugs in development.



❶ BINDING

HIV binds to the surface of a host cell.
ENTRY INHIBITORS, including these in development:

- **combinectin**

❷ FUSION

HIV's RNA reverse transcriptase, integrase, and other viral proteins fuse to the host cell.
FUSION INHIBITOR
MONOCLONAL ANTIBODIES (mAb) in development:

- **UB-421** (CD4 receptor)
- **VRC01** (CD receptor)
- **3BNC117/LS** and **10-1074/LS**
- **PGDM1400** and **PG121 10E8.4, etc.**
- **PRO-140** (CCR5 receptor)
- **albuvirtide**

❸ REVERSE TRANSCRIPTION

Viral DNA is formed by reverse transcription.
NRTIs and NRTTIs (nukes), including these in development:

- **islatravir**
- **MK-8504, MK-8583**

and NNRTIs, including these in development:

- **elsufavirine**

❹ INTEGRATION

Viral DNA is transported into the host cell's nucleus and integrates into the host's DNA.
INTEGRASE INHIBITORS

❺ REPLICATION

New viral RNA is used as genomic RNA and to make viral proteins.

❻ ASSEMBLY

New viral RNA and proteins move to the cell's surface; a new, immature (and non-infectious) virus forms.
PROTEASE INHIBITORS, including this one in development:

- **GS-1156**

❼ BUDDING

The virus becomes infectious when protease breaks up proteins in the immature virus to create the mature virus, that goes on to infect other CD4 cells.
CAPSID INHIBITOR in development:

- **GS-6207**

and MATURATION INHIBITOR in development:

- **GSK3640254, GSK '937**

SOURCES: PUBLIC HEALTH LIBRARY/CDC AND HIV i-BASE (i-BASE.INFO)
ILLUSTRATION BY ABBEY DENLINGER ©POSITIVELY AWARE

Getting around

In this guide, HIV drugs are grouped into eight categories
—plus, additional categories for select non-HIV drugs and PrEP

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

Biktarvy

BIC/FTC/TAF
bictegravir/emtricitabine/tenofovir alafenamide

★ Recommended initial regimen for most people

STANDARD DOSE

One tablet once daily without regard to food for people taking HIV treatment for the first time (treatment-naïve) or individuals with suppressed viral load on a stable HIV regimen with no history of treatment failure and no known resistance to components of the regimen: bictegravir, emtricitabine, or tenofovir. Tablet contains 50 mg of the INSTI bictegravir plus 200 mg emtricitabine and 25 mg TAF.

For adults and children weighing at least 55 pounds (25 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. Biktarvy is not recommended for people with CrCl less than 30 mL/min or people with severe liver impairment (see "More information").

- 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%). Six individuals in Study 1490 and none in Study 1489 stopped Biktarvy due to side effects, none of which were due to kidney problems. New data associate INSTIs and TAF with weight gain. See weight gain in "More information;" GO TO positivelyaware.com/articles/weighty-concerns and positivelyaware.com/articles/fatty-tissues. Serum creatinine, estimated creatinine clearance, urine glucose, and urine protein should be obtained before initiating Biktarvy and should be monitored during therapy. Bictegravir can cause a small, reversible increase in serum creatinine within the first few weeks of treatment that does not affect actual kidney function. There have been rare reports of depression and suicidal ideation, primarily among patients with a history of psychiatric illnesses, in people who are on 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 virus (HBV) infection. Severe exacerbations of hepatitis B have been reported in people co-infected with hepatitis B who have discontinued Biktarvy (due to elimination of the emtricitabine and TAF components, which also treat HBV). Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted upon Biktarvy discontinuation. Call your health care provider right away if you develop any of the following signs or symptoms of hepatitis: 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.

POTENTIAL DRUG INTERACTIONS

Do not take with rifampin or the anti-arrhythmic dofetilide (a heart medication). Not recommended to be taken with Cimduo or Temixys, Descovy, Emtriva, Epivir-HBV, Hepsera, Truvada, Vemlidy, or Viread, all for treatment of hepatitis B, as the emtricitabine and tenofovir components of Biktarvy already treat HBV. Biktarvy can be taken at least two hours before or six hours after taking laxatives or antacids, the ulcer medication sucralfate, oral iron or calcium supplements (but either of these two can be used with Biktarvy if taken with food at the same time), or buffered medications. Start metformin at lowest dose and titrate based on tolerability and clinical effect. 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. Not recommended with St. John's wort. 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

Biktarvy is widely prescribed because of its efficacy and safety profile as well as zero resistance emerging from use of this treatment. Weight gain, however, is being more commonly recognized as a potential side effect of INSTIs. In the community, enlargement of the stomach and waist area can be distressing. According to the DHHS HIV treatment guidelines, "Weight gain has been associated with initiation of ART [antiretroviral therapy] and subsequent viral suppression. The increase appears to be greater with INSTIs than with other drug classes. Greater weight increase has also been reported with TAF than with TDF, and greater with DOR than EFV." Other factors have been associated with weight gain in addition to medication used, including race, sex, and previous overweight status. There is no word yet on reversibility of weight gain, but the race is on to find more answers. The data show that the bictegravir drug resistance barrier is comparable to that of dolutegravir and ritonavir- or cobicistat-boosted protease inhibitors (such as darunavir in Prezista or Symtuza). That is a huge advantage. There are also now data supporting the use of Biktarvy in people with some resistance to its FTC component (the M184V change to HIV's genetic structure). Data are also accumulating that show Biktarvy works for people who have detectable virus when they switch to it from another regimen (having experienced virologic failure on their previous regimen). Biktarvy is a small INSTI-based STR tablet, which may help some individuals who have difficulty swallowing pills. Pediatric study is ongoing. At this time, there aren't sufficient data to support the use of Biktarvy during pregnancy. Although not part of the drug label, Biktarvy is regularly used without dose adjustment with hemodialysis, and there are data supporting that use.

Dr. Melanie Thompson: Biktarvy, a triple drug STR containing the INSTI bictegravir and 2 NRTIs, TAF and emtricitabine (FTC), is recommended for first-line initial therapy by DHHS and IAS-USA HIV guidelines, including for people with hepatitis B. (Remember that stopping Biktarvy can cause a hepatitis flair in people with hep B!) It has become a favorite for initial therapy because of its potency, high barrier to resistance, ability to take with or without food, and its small pill size. It also is a popular choice for rapid start of treatment before labs return. Bictegravir is not available as a stand-alone medication.

Biktarvy is generally well tolerated, but INSTIs and TAF both have been associated with weight gain, so discussions about diet and exercise are important, and weight should be monitored, although it is not clear that switching therapy reverses this problem after the fact. Bictegravir, like all INSTIs, also can be associated with insomnia and other nervous system side effects, including worsening of pre-existing depression.

Biktarvy can be taken with or without food, and drug interactions are fewer with Biktarvy than with boosted drugs or NNRTIs. There are still some important interactions, including contraindications for use with dofetilide and rifampin. The drug interaction with metformin is often underappreciated and should be managed carefully. As with all INSTIs, calcium, magnesium, zinc, aluminum, and iron supplements can lower levels of bictegravir and dosing recommendations should be followed.

Biktarvy should not be taken during pregnancy because of insufficient data. Someone who is contemplating pregnancy should begin another regimen, and pregnant persons on Biktarvy should change to another regimen for the duration of the pregnancy.

Activist Bridgette Picou: As a newer single-tablet regimen, Biktarvy is considered safe, tolerable, and effective. Used for both new starts and clinically stable patient switches, the pill size is quite manageable. There are some drug interactions, but overall, most patients find the medication easy to take. Keep an open line with your clinician about all medications you take.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$4,072.50/month

Triumeq

DTG/ABC/3TC
dolutegravir/abacavir/lamivudine

★ 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. 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). 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.

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. According to the drug label, Triumeq is not recommended for people who have decreased kidney function (creatinine clearance less than 50 mL/min) due to lamivudine component, or those with moderate or severe liver impairment due to abacavir component. This medication combination, however, is often used in reduced renal function below 50 mL/min, due to relatively minimal risk of lamivudine accumulation and side effects. In addition, alternative doses may be obtained by using the individual components of this medication as needed.

➤ 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. New data associate INSTIs with weight gain. See weight gain in "More information;" GO TO positivelyaware.com/articles/weighty-concerns and positivelyaware.com/articles/fatty-tissues. Dolutegravir can cause a small, reversible increase in serum creatinine within the first few weeks of treatment, but does not affect 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. DHHS guidelines recommend closely monitoring patients with pre-existing psychiatric conditions on an INSTI. Conflicting data suggest people who have a high risk for cardiovascular problems have a potential for heart problems when using abacavir-containing regimens. Monitor for signs of hypersensitivity reaction (HSR) to abacavir. Prior to starting Triumeq, all individuals should be given a simple 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 on the Ziagen page. Prior to initiation, people should be tested for hepatitis B virus (HBV) infection. Severe exacerbations of hepatitis B have been reported in people co-infected with hepatitis B who have discontinued Triumeq (due to elimination of the lamivudine component, which also treats HBV). Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted upon Triumeq discontinuation. Call your health care provider right away if you develop any of the following signs or symptoms of hepatitis: 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. See "More information" regarding pregnancy.

POTENTIAL DRUG INTERACTIONS

Do not take with the anti-arrhythmic dofetilide (a heart medication). Triumeq should be taken two hours before or six hours after taking antacids or laxatives, the ulcer medication sucralfate, 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, Nexium, Pepcid, Prevacid, Prilosec, and Zantac) 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 tolerability and clinical effect. 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. When taking rifampin, take an additional dose of dolutegravir (in the form of one Tivicay tablet) 50 mg 12 hours after taking your Triumeq dose. 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

Weight gain is becoming more widely recognized as a side effect of INSTIs. In the community, enlargement of the stomach and waist area can be distressing. According to DHHS HIV treatment guidelines, "Weight gain has been associated with initiation of ART [antiretroviral therapy] and subsequent viral suppression. The increase appears to be greater with INSTIs than with other drug classes." Other factors have been associated with weight gain in addition to medication used, including race, sex, and previous overweight status. There is no word yet on reversibility, but the race is on to find more answers. Dolutegravir is now a preferred medication at the time of conception as well as during pregnancy, per DHHS perinatal guidelines updated in December. See the onlline version of this page. 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). Triumeq has relatively few drug interactions and is well tolerated. Triumeq does not cover hepatitis B 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. Other STRs containing dolutegravir are Juluca and Dovato.

Dr. Melanie Thompson: Triumeq is recommended by DHHS and IAS-USA guidelines panels as a first-line initial therapy. It contains the INSTI dolutegravir and 2 NRTIs, abacavir and emtricitabine. Because of the risk of abacavir hypersensitivity (see Ziagen), a negative HLA B*5701 genetic test result must be obtained before starting an abacavir-containing regimen, so Triumeq cannot be used for rapid ART start. In addition, abacavir has been associated with cardiovascular disease in some, but not all, studies. It is generally not recommended for people with known heart disease or high risk for heart disease, when there are other options. Because Triumeq contains 3TC, which has activity against hepatitis B, stopping Triumeq can cause a flair of hepatitis B. Tenofovir (TAF or TDF) rather than lamivudine is recommended for persons with hepatitis B. Triumeq can be taken with or without food and is generally well tolerated, but some may experience insomnia or weight gain associated with dolutegravir. Calcium, magnesium, zinc, aluminum, and iron supplements can lower levels of all INSTIs and dosing recommendations should be observed. Updated data from the Botswana Tsempano study showed a very small increased risk of neural tube defects (birth defects affecting the developing nervous system) among infants of people who were taking dolutegravir when they became pregnant. Persons capable of pregnancy should discuss these issues with their providers before starting dolutegravir. (See Tivicay.) There have been no concerns about using dolutegravir in the second or third trimesters of pregnancy.

Activist Bridgette Picou: Triumeq can help you achieve your goal of viral suppression. A single tablet, it's potent, if a bit big. Before starting Triumeq, you will need a blood test to check for a genetic disposition that makes you vulnerable to a hypersensitive reaction. This is one of the reasons people shouldn't "borrow" a friend's medication. This can also develop after starting the pill. If it does, stop taking it and notify your clinician. Do not take Triumeq again in this situation. You will want to be monitored for heart and kidney function while on Triumeq. Insomnia and fatigue have been reported on Triumeq. Discuss risks and benefits with a clinician.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$3,818.26/month

Dovato

DTG/3TC
dolutegravir/lamivudine

★ Recommended initial regimen for most people except those with viral load greater than 500,000 copies/mL, hepatitis B virus (HBV) co-infection, or before results of genotypic resistance or HBV testing

STANDARD DOSE

One tablet once daily, without regard to food for treatment-naïve people who have no known resistance to components of the regimen: dolutegravir and lamivudine. 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. Dovato is not recommended for people who have severe liver impairment. According to the drug label, Dovato is not recommended for people with decreased kidney function (creatinine clearance less than 50 mL/min) due to the lamivudine component. This medication combination, however, is often used in reduced renal function below 50 mL/min, because of the relatively minimal risk of lamivudine accumulation and side effects. In addition, alternative doses may be obtained by using the individual components of this medication as needed.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Dolutegravir and lamivudine are both generally well tolerated. Side effects occurring in at least 2% of study participants receiving Dovato included headache, nausea, diarrhea, insomnia, fatigue, and dizziness. See weight gain in "More information;" GO TO positivelyaware.com/articles/weighty-concerns and positivelyaware.com/articles/fatty-tissues. Dolutegravir can cause a small, reversible increase in kidney function test (serum creatinine) within the first few weeks of treatment that does not affect 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. DHHS guidelines recommend closely monitoring patients with pre-existing psychiatric conditions on an INSTI. Prior to initiation, people should be tested for hepatitis B virus (HBV) infection. Severe exacerbations of hepatitis B have been reported in people co-infected with hepatitis B who have discontinued Dovato (due to elimination of the lamivudine component, which also treats HBV). Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted upon Dovato discontinuation. Call your health care provider right away if you develop any of the following signs or symptoms of hepatitis: 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.

POTENTIAL DRUG INTERACTIONS

Do not take Dovato with Epivir-HBV. When taking carbamazepine or rifampin, take an additional dose of dolutegravir (in the form of one Tivicay tablet) 50 mg 12 hours after taking your Dovato dose. When starting or stopping dolutegravir by people on metformin, dose adjustment of metformin may be necessary to maintain optimal glycemic control or tolerability. Avoid use of sorbitol-containing medicines with lamivudine; there are many, such as acetaminophen liquid (Tylenol liquid and others). There are no known drug-drug interactions 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

Approved in April 2019. Basically, this medicine is Triumeq without the abacavir component (brand name Ziagen, also found in Epzicom). Dolutegravir is from the powerhouse drug class of integrase inhibitors, which are highly effective and generally tolerable. The benefits of using a two-drug regimen for HIV include less exposure to HIV medication while maintaining viral suppression and minimizing the potential for side effects. At one, two, and nearly three years in the GEMINI-1 and GEMINI-2 studies, DTG plus 3TC was found to be non-inferior to the triple drug regimen of DTG plus Truvada (emtricitabine and tenofovir DF combined in one pill). At the 144-week point, for the two studies, 82% (584 out of 716 individuals) had undetectable viral load, compared to 84% (599 out of 717) of those taking the three-drug therapy. Everyone in the study was taking HIV treatment for the first time, and 20% of them had a high viral load of more than 100,000 copies per mL when entering the clinical trials. Dovato has also been successful for treatment-experienced people switching to it after being undetectable (viral load less than 50 copies per mL). The TANGO study evaluated treatment switch from TAF-containing regimens with three or more drugs to the 2-drug regimen of dolutegravir/lamivudine and, at both 48 and 96 weeks, found Dovato to be non-inferior to the three-drug regimen standard of care. Weight gain is being increasingly recognized as a side effect of INSTIs. In the community, enlargement of the stomach and waist area can be distressing. According to DHHS HIV treatment guidelines, "Weight gain has been associated with initiation of ART [antiretroviral therapy] and subsequent viral suppression. The increase appears to be greater with INSTIs than with other drug classes. Greater weight increase has also been reported with TAF than with TDF, and greater with DOR than EFV." Other factors have been associated with weight gain in addition to medication used, including race, sex, and previous overweight status. There is no word yet on reversibility, but the race is on to find more answers. Although dolutegravir is now a preferred medication during pregnancy as well as for those who are trying to conceive, U.S. HIV perinatal treatment guidelines suggest using three-drug regimens. Find the discussion on page C-51 of perinatal guidelines at hivinfo.nih.gov.

Dr. Melanie Thompson: Dovato, a two-drug combination of dolutegravir and lamivudine (3TC), is the only two-drug STR recommended for starting therapy. However, Dovato is not recommended if HIV RNA is greater than 500,000 c/mL or CD4 less than 200 cells/mL, or for people with hepatitis B. Therefore, Dovato is not ideal for rapid start of ART before viral load, CD4, resistance testing, and HBV serology are available. Resistance to 3TC would mean dolutegravir monotherapy, a strategy that is not recommended. While some maintain that it can still be used for rapid start, it will be necessary to modify treatment if 3TC mutations, HBV infection, high viral load, or low CD4 are detected on pre-treatment labs.

Last August, FDA also approved Dovato as a switch option for persons with undetectable virus who do not have hepatitis B or a history of viral resistance to its components. This opens up Dovato as an option for those who started ART before labs returned and who have no contraindications. A potential advantage of switching would be to limit exposure to fewer drugs and therefore possibly fewer side effects, while the primary downside would be lack of very long-term data about durability of the regimen in this setting.

The very small increased risk of neural tube defects associated with dolutegravir in the updated Tsempano study should be discussed with persons of childbearing potential before starting dolutegravir. (See Tivicay.)

While the cost of Dovato (Wholesale Acquisition Cost of $27,540) is lower than that of three- and four-drug STRs such as Biktarvy, Triumeq, and Symtuza, it is still quite high, especially considering that 3TC is one of our oldest ARV with a generic cost of about $500 per year. Let's work with Congress and the Biden administration to lower the cost of life-saving drugs for people with HIV!

Activist Bridgette Picou: The second two-drug, single-tablet therapy pill on the market, Dovato has an easy pill size, minimal side effects, and a high barrier to resistance. That, in addition to maintaining viral suppression on less drug over time, makes it an attractive pill option for people looking for less medication in the body. It also can be taken with or without food, unlike Juluca, which must be taken with a meal.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com; dovato.com;
(877) 844-8872

AVERAGE WHOLESALE PRICE

$3,032.81/month

Juluca

DTG/RPV
dolutegravir/rilpivirine

✔ Recommended as continuation therapy for people with undetectable HIV viral load for at least 6 months and do not have HBV co-infection.

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. New data associate INSTIs with weight gain; see "More information." GO TO positivelyaware.com/articles/weighty-concerns and positivelyaware.com/articles/fatty-tissues. 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.

POTENTIAL DRUG INTERACTIONS

Do not take Juluca with rifampin, rifapentine, or the anti-arrhythmic dofetilide (a heart medication). 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 H2 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. DHHS HIV treatment guidelines suggest that metformin be started at the lowest dose and titrated based on tolerability and clinical effect. Monitor for metformin adverse effects. When starting or stopping Juluca in people taking 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 was 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. People who are able to take their medications consistently as directed and achieve undetectable viral load can take advantage of this strategy with less exposure to HIV medications. 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 stages of the virus life cycle, similar to three-drug regimens. This is how the combination was used in clinical studies to date. DHHS guidelines listed this combination 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 except Dovato and Juluca contain two nucleoside drugs. Juluca contains two currently available medications. Weight gain is increasingly recognized as a side effect of INSTIs. In the community, enlargement of the stomach and waist area can be distressing. According to the DHHS HIV treatment guidelines, "Weight gain has been associated with initiation of ART [antiretroviral therapy] and subsequent viral suppression. The increase appears to be greater with INSTIs than with other drug classes. Greater weight increase has also been reported with TAF than with TDF, and greater with DOR than EFV." Other factors have been associated with weight gain in addition to medication used, including race, sex, and previous overweight status. There is no word yet on reversibility, but the race is on to find more answers. Juluca is the smallest STR, which may be advantageous to individuals who have difficulty swallowing. For individuals with HIV-2, commonly found outside the U.S., an NNRTI would not be recommended as HIV-2 is inherently resistant to NNRTIs. Rilpivirine is an alternative drug for use during pregnancy, and although dolutegravir is now a preferred medication in pregnancy as well as for those who are trying to conceive, U.S. HIV perinatal treatment guidelines suggest using three-drug regimens. Find the discussion on page C-51 of perinatal guidelines at hivinfo.nih.gov.

Dr. Melanie Thompson: Juluca, containing dolutegravir and the NNRTI rilpivirine, is a two-drug STR nuke-sparing regimen that was approved only for those whose virus is suppressed with no resistance to either drug. It is a reasonable and simple option for people who have extensive NRTI resistance from the earlier days, but whose virus is still sensitive to rilpivirine and dolutegravir. It also avoids nuke-related side effects.

Juluca does require attention to drug interactions. Proton-pump inhibitors (such as Prilosec and Nexium) reduce the absorption of rilpivirine and rifabutin requires a dose adjustment for rilpivirine. Dofetilide (for abnormal heart rhythm) and some seizure medications are contraindicated. In addition, supplements containing calcium, magnesium, zinc, aluminum, or iron can lower levels of dolutegravir, and dosing recommendations should be observed.

Juluca must be taken with at least 400 calories of solid food for rilpivirine absorption. This is important because rilpivirine has a low barrier to resistance, so adequate levels are essential.

It should be noted that kidney stones have been associated with rilpivirine.

The very small increased risk of neural tube defects associated with dolutegravir in the updated Tsempano study should be discussed with persons of childbearing potential. (See Tivicay.)

For a two-drug regimen, Juluca is fairly pricey.

Activist Bridgette Picou: While in the single-tablet regimen category, Juluca contains only two medications rather than three or four. It is used for patients who have been undetectable (virally suppressed) for at least 6 months. It should be taken with food in a meal containing at least 400 calories, and can be taken at any time of day.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com; juluca.com;
(877) 844-8872

AVERAGE WHOLESALE PRICE

$3,578.52/month

Symtuza

DRV/COBI/FTC/TAF
darunavir/cobicistat/emtricitabine/tenofovir alafenamide

✔ Recommended initial regimen in certain clinical situations

STANDARD DOSE

One tablet once daily with food for treatment-naïve individuals or individuals 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, boosted by 150 mg cobicistat, with 200 mg emtricitabine and 10 mg TAF.

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. Symtuza can be used by people with an estimated creatinine clearance of at least 30 mL/ min. It should not be used by people who have severe kidney or liver impairment. Symtuza is not recommended during pregnancy due to substantially lower exposures of darunavir and cobicistat components during pregnancy.

- SEE THE INDIVIDUAL DRUGS CONTAINED IN SYMTUZA: Prezista, Tybost, and 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 studies include diarrhea (9%), rash (8%), nausea (6%), fatigue (4%), headache (3%), abdominal discomfort (2%), and flatulence (2%). While very rare (in less than 0.4% of those taking it), severe rash, accompanied in some cases by fever and/or elevations of AST/ALT (liver enzymes), can be life-threatening. Seek medical attention immediately. New data associate TAF with weight gain. See the online version of this drug page. Observational cohort studies reported an association between some PIs (including darunavir taken with ritonavir) and an increased risk of cardiovascular (CV) events. Data with darunavir plus cobicistat are too limited to make these conclusions. 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). While cobicistat does not affect actual kidney function, its effect on SCr can make monitoring of impaired kidney function more difficult or less accurate. However, people 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 virus (HBV) infection. Severe exacerbations of hepatitis B have been reported in people co-infected with hepatitis B who have discontinued Symtuza (due to elimination of the emtricitabine and TAF components, which also treat HBV). Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted upon Symtuza discontinuation. Call your health care provider right away if you develop any of the following signs or symptoms of hepatitis: 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.

POTENTIAL DRUG INTERACTIONS

Do not take with Cimduo or Temixys, Descovy, Emtriva, Epivir-HBV, Hepsera, Truvada, Vemlidy, or Viread, all used for the treatment of hepatitis B. Use with other protease inhibitors or Intelence, Sustiva, or Viramune is not recommended. Do not take with alfuzosin, betamethasone, budesonide, carbamazepine, dexamethasone, dronedarone, eslicarbazepine, ergot derivatives, fluticasone, triazolam, oral midazolam, lomitapide, lurasidone, methylprednisolone, naloxegol, oxcarbazepine, phenobarbital, phenytoin, pimozide, Revatio, simvastatin, lovastatin, St. John's wort, ranolazine, or rifampin. Not recommended to be taken with avanafil, ciclesonide, dabigatran etexilate (in renal impairment), everolimus, Intelence, irinotecan, mometasone, rifabutin, rifapentine, rivaroxaban, salmeterol, ticagrelor, triamcinolone, or voriconazole. 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. Apixaban (Eliquis) dose may need to be adjusted. Do not take with colchicine if there is kidney or liver impairment. Start metformin at lowest dose and titrate based on tolerability and clinical effect. Cannot be taken with Zepatier. Based on the mechanism, drug interactions with other hepatitis C medications are probably similar to the interactions with Prezcobix + 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

Symtuza is the first STR containing a protease inhibitor. This formulation is much more convenient and reduces the number of co-pays to one. It is not the same as Prezcobix plus Descovy, because Symtuza contains a lower dose of TAF than Descovy. 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. 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. Melanie Thompson: Symtuza, a four-drug STR, is the only single-tablet regimen containing a protease inhibitor (darunavir). DHHS guidelines recommend it as initial therapy only "in certain clinical situations" when an INSTI cannot be used, largely because it contains cobicistat as a booster. It has a long laundry list of drug-drug interactions associated with both cobicistat and darunavir and also has the potential to raise triglycerides and cholesterol. (See Prezista and Tybost.) On the positive side, it does have a high barrier to resistance, thanks to boosted darunavir. A single-arm study sponsored by Janssen showed favorable outcomes when Symtuza was used as rapid ART prior to the return of baseline labs. The drug was effective even when certain drug resistance mutations were present.

Symtuza is the most expensive STR, with a Wholesale Acquisition Cost (WAC) of over $42K. Although patient assistance copays may take the sting out of the actual out-of-pocket cost for consumers, it's very hard to justify the astronomic cost when less expensive and equally effective regimens are available. Even the separate components are cheaper than the STR. Again, time to advocate for controls on HIV (and other) drug prices. Symtuza should not be taken by persons who are pregnant, due to insufficient levels associated with cobicistat.

Activist Bridgette Picou: Symtuza can be used in both initial ART therapy and in patients who are stable and whom have achieved viral suppression. This STR contains a protease inhibitor component, making it different from other single-tab regimens. Darunavir, the main component in Symtuza, has a high barrier to resistance, which you want in a medication. Take it with food; discuss all your medications with your clinician to avoid drug-drug interactions, since Symtuza also contains a booster.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$4,877.76/month

Delstrigo

DOR/3TC/TDF
doravirine/lamivudine/tenofovir disoproxil fumarate

✔ Recommended initial regimen in certain clinical situations

STANDARD DOSE

One tablet once daily without regard to food for people taking HIV treatment for the first time (treatment-naïve) or individuals with suppressed viral load on a stable HIV regimen for at least 6 months who have no known resistance to components of the regimen: doravirine, lamivudine, or tenofovir. 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 for people with estimated creatinine clearance less than 50 mL/min. Should not be used by people with moderate or severe kidney impairment or severe liver impairment.

- SEE THE INDIVIDUAL DRUGS CONTAINED IN DELSTRIGO: Pifeltro, Epivir, and Viread.
- 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 were dizziness (7%), nausea (5%), abnormal dreams (5%), and headache (4%). Neuropsychiatric events—such as depression, sleep disturbances, dizziness, etc.—are another common side effect of the NNRTI drug class. The proportion of people who reported one or more neuropsychiatric adverse events overall was 24% for the Delstrigo group compared to 57% for the Atripla group in the DRIVE-AHEAD study. 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 experienced by 9% of 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 those on Atripla. 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 people on TDF-containing regimens. BMD monitoring should be considered for 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. Prior to initiation, people should be tested for hepatitis B virus (HBV) infection. Severe exacerbations of hepatitis B have been reported in people co-infected with hepatitis B who have discontinued Delstrigo (due to elimination of the lamivudine and TDF components, which also treat HBV). Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted upon Delstrigo discontinuation. Call your health care provider right away if you develop any of the following signs or symptoms of hepatitis: 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.

POTENTIAL DRUG INTERACTIONS

Do not take with Cimduo or Temixys, Descovy, Emtriva, Epivir-HBV, Hepsera, Truvada, Vemlidy, or Viread, all 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 100 mg tablet approximately 12 hours later. Avoid taking Delstrigo with drugs that negatively affect the kidneys, including chronic use or high doses of anti-inflammatory drugs for pain such as Advil or Motrin (ibuprofen) and Aleve (naproxen). 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 (a 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, Temixys) are also approved; see those pages. Unfortunately, Delstrigo contains an older prodrug of tenofovir, TDF. A safer version, TAF, is available and used in some STRs. Ironically, however, as TAF and INSTIs may have some association with weight gain, Delstrigo may become a more popular option. (See Tivicay; also, GO TO positivelyaware.com/articles/weighty-concerns and positivelyaware.com/articles/fatty-tissues.) TDF is still an effective and quite tolerable medication, but TAF has potentially less long-term renal and bone toxicity. Doravirine has not been directly compared to integrase inhibitor-based regimens in clinical trials yet. For individuals with HIV-2, commonly found outside the U.S., an NNRTI would not be recommended as HIV-2 is inherently resistant to NNRTIs. There are no data on the safe use of Delstrigo during pregnancy.

In the DRIVE-FORWARD study comparing doravirine to darunavir, at 96 weeks, 72% of treatment-naïve individuals in the doravirine group attained undetectable status (a viral load of less than 50 copies/mL), compared to 65% for the darunavir group.

Dr. Melanie Thompson: Delstrigo is an STR containing doravirine (DOR), the newest NNRTI, as well as generic 3TC and TDF. DOR has not been compared directly with any INSTI-containing regimens, therefore it is not a recommended option for most people starting therapy according to DHHS and IAS-USA guidelines. It is, however, recommended "in certain situations" when an INSTI can't be used. Finding a niche for an NNRTI-based regimen is a bit of a challenge these days. Delstrigo was found to be non-inferior to efavirenz, which now is rarely prescribed to anyone who is not still clinging to their Atripla, but DOR + nukes also was non-inferior to ritonavir-boosted darunavir. It could possibly be an option for people on a boosted PI regimen without substantial viral resistance to NNRTIs and NRTIs and who could benefit from getting away from a boosted regimen.

Delstrigo is well tolerated and DOR has the advantage of having fewer and less severe central nervous system side effects than efavirenz. It also has no food requirements.

An analysis of weight gain on DOR-containing regimens found no difference between DOR, ritonavir-boosted darunavir, and efavirenz after nearly 2 years.

Delstrigo should not be prescribed to anyone who is pregnant as there are insufficient data on pregnancy.

The inclusion of generic drugs allows Delstrigo to be priced lower than other three- or four-drug STRs, although one can certainly argue that the price could be substantially lower because of the generic components.

Activist Bridgette Picou: Delstrigo can be taken with or without regard to food. When taking Delstrigo, you should be tested for hepatitis B virus (HBV). While having HBV does not preclude you from taking the medication, you need to know your status so that you do not suddenly stop taking it, as this can cause a flare in your HBV. Take missed doses as soon as possible, as with all HIV meds, and do not double up on missed ones. Should you find yourself running low or know you may be without medication, speak with your clinician or a case management specialist for options.

MANUFACTURER

Merck and Co.
delstrigo.com; (800) 672-6372

AVERAGE WHOLESALE PRICE

$2,778.12/month

Genvoya

EVG/COBI/FTC/TAF
elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide

✔ Recommended initial regimen in certain clinical situations

STANDARD DOSE

One tablet once daily with food. For people taking HIV treatment for the first time (treatment-naïve) or individuals with suppressed viral load on a stable HIV regimen for at least 6 months who have no known resistance to the elvitegravir, emtricitabine, or tenofovir components of this regimen. 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 (CrCl) 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 people on chronic hemodialysis, take tablet once daily and administer 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. (TAF is not available separately for HIV, but is used to treat hepatitis B under the brand name Vemlidy.)

➤ 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. New data associate INSTIs and TAF with weight gain; GO TO positivelyaware.com/articles/weighty-concerns and positivelyaware.com/articles/fatty-tissues, and hivinfo.nih.gov. Before taking Genvoya, kidney function testing should be conducted, including serum creatinine (SCr), 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). While cobicistat does not affect actual kidney function, its effect on SCr can make monitoring of impaired kidney function more difficult or less accurate. INSTIs have been associated with adverse neuropsychiatric effects (such as sleep disturbances, depression, anxiety, suicidal ideation) in some retrospective cohort studies and case series. DHHS guidelines recommend closely monitoring patients on an INSTI who have pre-existing psychiatric conditions. Prior to initiation, people should be tested for hepatitis B virus (HBV) infection. Severe exacerbations of hepatitis B have been reported in people co-infected with hepatitis B who have discontinued Genvoya (due to elimination of the emtricitabine and TAF components, which also treat HBV). Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted upon Genvoya discontinuation. Call your health care provider right away if you develop any of the following signs or symptoms of hepatitis: 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.

POTENTIAL DRUG INTERACTIONS

Do not take with Cimduo or Temixys, Descovy, Emtriva, Epivir-HBV, Hepsera, Truvada, Vemlidy, or Viread, all 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 Aciphex, Dexilant, 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, methyl-ergonovine, oral midazolam, lurasidone, pimozide, Revatio, rifampin, rifabutin, rifapentine, Serevent, triazolam, St. John's wort, clopidogrel, or ticagrelor. 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. Start metformin at lowest dose and titrate based on tolerability and clinical effect. Reduce Daklinza dose to 30 mg. Can be taken with Harvoni or Epclusa. Taking with Olysio, Viekira Pak, or Zepatier is not recommended. 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. Melanie Thompson: Genvoya, an INSTI-based four-drug regimen, is basically Stribild with TAF substituted for TDF. Other drugs are emtricitabine (FTC) and the INSTI elvitegravir boosted by cobicistat. Cobicistat's high potential for drug interactions, as well as lipid effects, and the relative fragility of elvitegravir to viral resistance have downgraded Genvoya to the level of an alternative in certain situations when non-boosted INSTI regimens cannot be used. It is increasingly difficult to imagine any reason to prefer Genvoya over non-boosted INSTI drugs.

Because so many people with HIV have other conditions for which they take medications, avoiding boosters like cobicistat helps to decrease drug interactions that could cause toxicity. In particular, dosing of common drugs such as statins, metformin, and steroids require close attention with boosters.

Although INSTIs are associated with more weight gain than PIs and NNRTIs, elvitegravir is associated with the least weight gain among INSTIs. Genvoya, however, also contains TAF, which has been associated with more weight gain than TDF in some studies.

Activist Bridgette Picou: Genvoya should be taken with food. The pill contains a booster, cobicistat, and is metabolized in the liver, so you will need to monitor for kidney toxicity and drug-drug interactions. Still, it is considered more friendly than its closest cousin, Stribild. Among the drugs to monitor for interactions are statins, erectile dysfunction medications, and some of the mood stabilizers. Be sure to let your HIV provider know if you start or stop any of these.

MORE INFORMATION

Weight gain is being more commonly recognized as a potential side effect of INSTIs. In the community, enlargement of the stomach and waist area can be distressing. According to the DHHS HIV treatment guidelines, "Weight gain has been associated with initiation of ART [antiretroviral therapy] and subsequent viral suppression. The increase appears to be greater with INSTIs than with other drug classes. Greater weight increase has also been reported with TAF than with TDF, and greater with DOR than EFV." Other factors have been associated with weight gain in addition to medication used, including race, sex, and previous overweight status. There is no word yet on reversibility, but the race is on to find more answers. Genvoya is not recommended during pregnancy due to substantially lower exposures of cobicistat and elvitegravir in the second and third trimesters as well as reports of viral breakthrough. Switching regimens should be considered for pregnant women already taking this regimen.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$4,072.50/month

Stribild

EVG/COBI/FTC/TDF
elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate

✔ Recommended initial regimen in certain clinical situations

STANDARD DOSE

One tablet once daily with food. For people taking HIV therapy for the first time (treatment-naïve) or people with suppressed viral load on a stable HIV regimen for at least 6 months who have no known resistance to the elvitegravir, emtricitabine, or tenofovir components of the regimen. Tablet contains 150 mg of the INSTI elvitegravir boosted by 150 mg cobicistat plus 200 mg emtricitabine and 300 mg tenofovir DF (TDF).

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 by 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. New data associate INSTIs and TAF with weight gain; see "More information," and GO TO positivelyaware.com/articles/weighty-concerns and positivelyaware.com/articles/fatty-tissues. The TDF in Truvada is associated with long-term decreases in bone mineral density (BMD). BMD monitoring should be considered for 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. 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 that does not affect 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. Prior to initiation, people should be tested for hepatitis B virus (HBV) infection. Severe exacerbations of hepatitis B have been reported in people co-infected with hepatitis B who have discontinued Stribild (due to elimination of the emtricitabine and TDF components, which also treat HBV). Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted upon Stribild discontinuation. Call your health care provider right away if you develop any of the following signs or symptoms of hepatitis: 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.

POTENTIAL DRUG INTERACTIONS

Do not take with Cimduo or Temixys, Descovy, Emtriva, Epivir-HBV, Hepsera, Truvada, Vemlidy, or Viread, all 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 Aciphex, Dexilant, Nexium, Pepcid, Prevacid, Prilosec, and Zantac. Do not take Stribild with alfuzosin, carbamazepine, phenobarbital, phenytoin, ergotamine, dihydroergotamine, methyl-ergonovine, 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 such as digoxin. Stribild increases levels of many nasal and inhaled steroids such as 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 such as Prograf, Gengraf, Neoral, and Sandimmune with caution. Start metformin at lowest dose and titrate based on tolerability and clinical effect. Reduce Daklinza dose to 30 mg. Taking with Harvoni, Olysio, Viekira Pak, or Zepatier is not recommended. Monitor kidney function more closely 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 many other drug interactions not listed here.

Dr. Melanie Thompson: Stribild was the first four-drug INSTI regimen to be approved for treatment. Like Genvoya, it contains cobicistat-boosted elvitegravir and emtricitabine, but with TDF. Also, like Genvoya, it is no longer recommended for initial therapy for most persons, largely because of the drug-drug interactions and lipid effects of cobicistat, and the genetic fragility of elvitegravir. Notably, boosting has been shown to exacerbate toxicities of TDF.

Because both TDF and TAF are recommended NRTIs, Genvoya and Stribild are treated as equals by the DHHS guidelines, although they might be used in different populations because of their side effects.

Although INSTIs are associated with more weight gain than PIs and NNRTIs, elvitegravir is associated with the least weight gain among INSTIs. The inclusion of TDF in Stribild likely decreases weight, so it counterbalances INSTI effects to some degree.

Stribild cannot be used in pregnancy because of inadequate drug levels associated with cobicistat.

Stribild still carries a high price tag, in spite of containing TDF, which is now generic.

Activist Bridgette Picou: If taking Stribild, you should have baseline kidney function testing done, and monitor throughout its use. The tenofovir DF component also means bone density testing is a good idea. Stribild needs to be taken with food. You and your clinician should keep an open dialog about other medications prescribed to avoid drug to drug interactions.

MORE INFORMATION

Weight gain is increasingly recognized as a potential side effect of INSTIs. In the community, enlargement of the stomach and waist area can be distressing. According to the DHHS HIV treatment guidelines, "Weight gain has been associated with initiation of ART [antiretroviral therapy] and subsequent viral suppression. The increase appears to be greater with INSTIs than with other drug classes. Greater weight increase has also been reported with TAF than with TDF, and greater with DOR than EFV." Other factors have been associated with weight gain in addition to medication used, including race, sex, and previous overweight status. No word yet if it is reversible, but the race is on to find more answers. Stribild is not recommended for use during 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.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$4,272.06/month

Odefsey

RPV/FTC/TAF
rilpivirine/emtricitabine/tenofovir alafenamide

✔ Recommended initial regimen in certain clinical situations

STANDARD DOSE

One tablet once daily, with a standard meal. For people taking HIV therapy for the first time (treatment-naïve) or people with suppressed viral load on a stable HIV regimen for at least six months who have no known resistance to the components of the regimen: rilpivirine, emtricitabine, or TAF. See below. Tablet contains 25 mg of the NNRTI rilpivirine plus 200 mg emtricitabine and 25 mg tenofovir alafenamide (TAF).

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, or people with a CrCl less than 15 mL/min who are receiving dialysis.

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

According to DHHS guidelines, people taking HIV treatment for the first time should have an HIV RNA (viral load) of less than 100,000 copies/mL and CD4 T cell count must be above 200 cells/mm^3 before starting Odefsey due to higher rates of virologic failure in these patients. The CD4 requirement, however, is no longer on the drug label.

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 (coformulation 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, angioedema (swelling), urticaria (itchy rash), and increased liver enzymes have also been reported with regimens containing rilpivirine. New data associate TAF with potential weight gain; see "More information." GO TO positivelyaware.com/articles/weighty-concerns and positivelyaware.com/articles/fatty-tissues. 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 observed 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 virus (HBV) infection. Severe exacerbations of hepatitis B have been reported in people co-infected with hepatitis B who have discontinued Odefsey (due to elimination of the emtricitabine and TAF components, which also treat HBV). Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted upon Odefsey discontinuation. Call your health care provider right away if you develop any of the following signs or symptoms of hepatitis: 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.

POTENTIAL DRUG INTERACTIONS

Do not take with Cimduo or Temixys, Descovy, Emtriva, Epivir-HBV, Hepsera, Truvada, Vemlidy, or Viread, all used for the treatment of hepatitis B. Proton pump inhibitors (PPIs, heartburn or stomach acid drugs like Aciphex, Dexilant, Nexium, Prevacid, Prilosec, Protonix, etc.) cannot 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 such as 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 taken with fluconazole, itraconazole, ketoconazole, posaconazole, or 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. Odefsey should not be taken with other medications that prolong QTc interval (a heart problem) or medications with a known risk for torsades de pointes. May be taken with Harvoni, Zepatier, or 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 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. Weight gain is increasingly recognized as a side effect of TAF. In the community, enlargement of the stomach and waist area can be distressing. According to the DHHS HIV treatment guidelines, "Weight gain has been associated with initiation of ART [antiretroviral therapy] and subsequent viral suppression. The increase appears to be greater with INSTIs than with other drug classes. Greater weight increase has also been reported with TAF than with TDF, and greater with DOR than EFV." Other factors have been associated with weight gain in addition to medication used, including race, sex, and previous overweight status. There is no word yet on reversibility, but the race is on to find more answers. For individuals with HIV-2, more commonly found outside the U.S., an NNRTI would not be recommended as HIV-2 is inherently resistant to NNRTIs. Pregnant patients virologically suppressed on Odefsey may continue taking it. Lower exposures of rilpivirine were observed during pregnancy, therefore viral load should be monitored closely.

Dr. Melanie Thompson: Odefsey is Complera with TAF instead of TDF. It also contains the NNRTI rilpivirine, which has fewer side effects than efavirenz, and the NRTI emtricitabine (FTC).

Like Complera, Odefsey is recommended for initial therapy only in "certain situations" when INSTI-based treatment cannot be used. While kidney and bone side effects are a consideration with TDF, there are now concerns about weight gain with TAF, as well as mildly elevated lipids. For people just starting therapy, I see little role for either Odefsey or Complera these days.

There are a number of notable drawbacks to rilpivirine. (See Edurant.) Rilpivirine is recommended only when viral load is less than 100,000 copies/mL and CD4 T cell count must be above 200 cells/mm^3. It should not be used with proton-pump inhibitors such as Prilosec and Nexium, and dosing must be managed if taken with other acid-blockers. It also has been associated with kidney stones.

Odefsey carries a high price tag, requiring a copay card to partially defray out-of-pocket costs in order to be affordable.

Activist Bridgette Picou: Most comparable to Complera, Odefsey is a once-daily, single-tablet pill. It is a switch option for patients stable on other ART and for people whose viral load is less than 100,000, and can be used for initial therapy. Using TAF instead of TDF means less toxicity to the kidneys, and less damage to the bones, but both should still be followed. If you take antacids for heartburn, let your provider know. Additionally, if you feel depressed or hopeless while taking Odefsey, speak to your health-care provider.

MANUFACTURERS

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

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

AVERAGE WHOLESALE PRICE

$3,706.28/month

Complera

RPV/FTC/TDF
rilpivirine/emtricitabine/tenofovir disoproxil fumarate

✔ Recommended initial regimen in certain clinical situations

STANDARD DOSE

One tablet once daily, with a standard meal. For people taking HIV therapy for the first time (treatment-naïve) or people with suppressed viral load on a stable HIV regimen for at least 6 months who have no known resistance to the components of the regimen: rilpivirine, emtricitabine, or tenofovir. Tablet contains 25 mg of the NNRTI rilpivirine plus 200 mg emtricitabine and 300 mg tenofovir DF (TDF).

For adults and children 12 years of age and older weighing at least 77 pounds (35 kg) and having a CrCl of at least 50 mL/min.

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

According to DHHS guidelines, people taking HIV treatment for the first time should have an HIV RNA (viral load) of less than 100,000 copies/mL and CD4 T cell count must be above 200 cells/mm^3 before starting Complera due to higher rates of virologic failure in these patients. The CD4 requirement, however, is no longer on the drug label.

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, angioedema (swelling), urticaria (itchy 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. The TDF in Complera 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. See Truvada page for other possible effects on kidney function. Prior to initiation, people should be tested for hepatitis B virus (HBV) infection. Severe exacerbations of hepatitis B have been reported in people co-infected with hepatitis B who have discontinued Complera (due to elimination of the emtricitabine and TDF components, which also treat HBV). Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted upon Complera discontinuation. Call your health care provider right away if you develop any of the following signs or symptoms of hepatitis: 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.

POTENTIAL DRUG INTERACTIONS

Do not take with Cimduo or Temixys, Descovy, Emtriva, Epivir-HBV, Hepsera, Truvada, Vemlidy, or Viread, all 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 such as 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 (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, or 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 for torsades de pointes. Complera may be taken with Harvoni and Zepatier. Monitor for tenofovir toxicities 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 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. TAF, however, is now associated with weight gain, more so than TDF. 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. For individuals with HIV-2, more commonly found outside the U.S., an NNRTI would not be recommended as HIV-2 is inherently resistant to NNRTIs. For pregnant patients who are already on Complera prior to pregnancy and who are virologically suppressed, one tablet taken once daily may be continued. Lower exposures of rilpivirine were observed during pregnancy, therefore viral load should be monitored closely.

Dr. Melanie Thompson: Complera quickly gained popularity as a replacement for Atripla, with fewer central nervous system side effects associated with rilpivirine than efavirenz. It also contains FTC and TDF. (See Truvada.) Because of the genetic fragility, multiple drug side effects, and decreased effectiveness at high viral loads or low CD4 counts, rilpivirine-containing regimens are not recommended for initial therapy unless INSTIs cannot be taken. (See Edurant.) As mentioned for Odefsey, there is little role for Complera in initial therapy in 2021.

Because TAF has less effect on kidney function and bone density, many people switched from Complera to Odefsey. However, we now know that weight gain and lipids are higher on TAF, although we don't know the clinical meaning of these findings in terms of risk for cardiovascular and other diseases. Lipids also are lower with TDF than TAF.

Complera carries a very high price tag, in spite of containing TDF, now off patent. Can we please do better?

Activist Bridgette Picou: Three medications in one tablet, Complera is taken once daily with a meal you chew, not simply a shake or protein drink. Consider that, and the time of day you dose, if you take antacids for heartburn. Indicated for patients who have a suppressed viral load (undetectable) at least 6 months, or for treatment-naïve patients. There should also be no known resistance to any of its components. Complera contains tenofovir disoproxil fumarate, which means regular testing of bone density and kidney function should be conducted.

MANUFACTURERS

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

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

AVERAGE WHOLESALE PRICE

$3,706.28/month

Atripla

EFV/FTC/TDF
efavirenz/emtricitabine/tenofovir disoproxil fumarate

✔ Recommended initial regimen in certain clinical situations

STANDARD DOSE

One tablet once daily on an empty stomach, preferably at bedtime (food can increase the risk of central nervous system, or CNS, side effects). 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; Atripla should not be used in people with moderate or severe kidney or liver impairment. Atripla is not recommended for people with CrCl less than 50mL/min or individuals requiring dialysis.

Other similar, but not exact, medications are also available (see page 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 reviewed four previously published AIDS Clinical Trials Group (ACTG) studies regarding efavirenz and suicidal ideation and re-emphasized an association between efavirenz and 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. The TDF in Atripla 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 who 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. 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 virus (HBV) infection. Severe exacerbations of hepatitis B have been reported in people co-infected with hepatitis B who have discontinued Atripla (due to elimination of the emtricitabine and TDF components, which also treat HBV). Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted upon Atripla discontinuation. Call your health care provider right away if you develop any of the following signs or symptoms of hepatitis: 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. 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 component in Atripla can cause a false positive result for marijuana on certain drug tests. A more specific confirmatory test can be done. See weight discussion in the onine version of this page.

POTENTIAL DRUG INTERACTIONS

Do not take with Cimduo or Temixys, Descovy, Emtriva, Epivir-HBV, Hepsera, Truvada, Vemlidy, or Viread, all used for the treatment of hepatitis B. Avoid taking 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). 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 for torsades de pointes. For patients weighing at least 110 pounds (50 kg) and taking rifampin, it is recommended to give 200 mg of efavirenz in addition to Atripla (for a total efavirenz dose of 800 mg per day). 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 using other contraceptive methods. 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. Cardizem, Lipitor, Pravachol, and Zocor doses may need to be adjusted. Titrate dose of bupropion and sertraline based on clinical response. 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 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. Melanie Thompson: Atripla (efavirenz/TDF/FTC) was the first complete one pill STR and revolutionized therapy as much as it simplified it. Unfortunately, efavirenz causes a raft of side effects (see Sustiva), some serious (such as suicidality), and is no longer recommended as first-line therapy. There is some role for efavirenz in the treatment of tuberculosis when rifampin must be taken, but now we know that dolutegravir can be taken twice daily in this setting, making it less likely that Atripla would be used in this setting.

Activist Bridgette Picou: Atripla is what I would call a "mixed bag" medication. It was the first STR and once a favorite for initial therapy. While effective, the drug had a host of neurotoxic side effects like vivid dreams, a sensation of being in a fog, fatigue, and depression. Despite this, many patients credit it with saving their life. I distinctly remember early on in my nursing career, patients were reluctant to switch from Atripla, even with the side effects, because it worked. If used, it should be taken on an empty stomach at bedtime.

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. Check with your provider or pharmacist first when stopping Atripla, so that you avoid the rapid development of HIV resistance to it. Many individuals switching from Atripla to a new regimen report never realizing what a fog they had been living under. For individuals with HIV-2, more commonly found outside the U.S., an NNRTI such as efavirenz would not be recommended as HIV-2 is inherently resistant to NNRTIs.

MANUFACTURERS

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

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

AVERAGE WHOLESALE PRICE

$3,593.65/month
generic: **$3,413.97**/month

Symfi and  Symfi Lo

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

✔ 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, side effects). 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 AND SYMFI LO:** Sustiva, Epivir, and Viread. See also similar STR, Atripla.

➤ **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 (physical weakness or lack of energy, 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 receiving mental health care. See also similar STR, Atripla. Common side effects may include dizziness, drowsiness, abnormal or vivid dreams, difficulty concentrating, rash, diarrhea, nausea, fatigue, headache, and insomnia. These side effects may disappear after a few weeks. The TDF in Symfi and in Symfi Lo is associated with long-term decreases in bone mineral density (BMD). BMD monitoring should be considered for 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. 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 HBV have been reported in people who are co-infected with hepatitis B and have discontinued emtricitabine and/or tenofovir, both if which treat HBV. Monitor liver enzymes closely in people co-infected with HBV and, if appropriate, initiation of anti-hepatitis B therapy may be warranted. The efavirenz component of Symfi and of Symfi Lo 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. See discussion on the Atripla page. The efavirenz component in Symfi and in Symfi Lo can cause a false positive result for marijuana on certain drug tests. A more specific confirmatory test can be done. See weight gain in the online versin of this page. GO TO positivelyaware.com/articles/weighty-concerns and positivelyaware.com/articles/fatty-tissues.

POTENTIAL DRUG INTERACTIONS

Do not take with Cimduo/Temixys, Descovy, Emtriva, Epivir-HBV, Hepsera, Truvada, Vemlidy, or Viread, all 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 for torsades de pointes. For patients weighing at least 110 pounds (50 kg) and taking rifampin, it is recommended to give a 200 mg efavirenz dose (for total efavirenz dose of 800 mg). 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. May decrease effectiveness of birth control pills; consider the use of other contraceptive methods. 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. Should not be taken with Epclusa 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. Melanie Thompson: For the first time, we now have two fully generic single-tablet-regimens, both with efavirenz (two doses, 400 mg and 600 mg), tenofovir disoproxil fumarate, and emtricitabine. Sadly, they are a decade too late to be useful, as the toxicity of efavirenz has resulted in its demotion to a rarely prescribed drug. In fairness, the 400 mg dose in Symfi Lo is associated with less toxicity, but why would you want to take it with better drugs available?

Activist Bridgette Picou: To be honest, I had never heard of Symfi or Symfi Lo until last year. Most closely comparable to Atripla, they use lamuvidine in place of emtricitabine. Symfi Lo has a lower dose of efavarenz, which would mean fewer neuro effects such as depression and insomnia. While taking these medications, self-check and monitor for these types of symptoms. Rash is a common side effect that will usually resolve on its own. If anything, the benefit would be that these drugs are a lower cost option than comparable medications on the market.

MORE INFORMATION

Symfi and Symfi Lo are basically alternative versions of Atripla, a medication that's no longer preferred when starting therapy. The advantage is they may be a cheaper alternative than some first-line medications because their components are all available as generics. If you can't sleep, ask your doctor about gradually adjusting the timing of your dose until it's taken during the day. A 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 along with fewer side effects. Symfi Lo is now approved in the U.S. for initial treatment of HIV infection (although guidelines no longer list it as a preferred option for someone starting medication). There is a discussion of the data on page G-31 of DHHS guidelines. Symfi and Symfi Lo are listed as a "Recommended Regimen in Certain Clinical Situations" in the DHHS guidelines, as is Atripla, 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 rapid development of HIV resistance to them—check with your provider or pharmacist first.

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

Cabenuva

CAB LA / RPV LA
cabotegravir extended-release injectable suspension;
rilpivirine extended-release injectable suspension

● DHHS recommendation not yet established at time of publication

STANDARD DOSE

Two long-acting intramuscular gluteal (butt muscle) injections once monthly. Consists of one injection of long-acting cabotegravir and one injection of long-acting rilpivirine. No food restrictions.

For adults switching from a stable HIV regimen who have undetectable viral load (less than 50 copies per mL) with no history of antiretroviral treatment failure and no drug resistance or suspected resistance to cabotegravir or rilpivirine. A month of daily oral lead-in therapy is required before injections begin, consisting of a 30 mg tablet of cabotegravir (Vocabria) and a 25 mg tablet of rilpivirine (Edurant). Oral rilpivirine must be taken with food; the injectable does not. Initiate injections on last day of oral lead-in. If up to eight weeks of treatment is missed (four injections total), restart therapy with the maintenance dose of 400 mg CAB LA plus 600 mg RPV LA. If more than eight weeks of therapy has been missed, restart treatment with the higher initial dose of 600 mg CAB LA plus 900 mg RPV LA, then continue with the lower doses thereafter. The oral medications can also be used as "bridging" if shots cannot be obtained on time. Increased monitoring is recommended when CrCl is less than 30. The effect of severe liver impairment on Cabenuva is unknown.

➤ **SEE EDURANT;** Vocabria is not available separately

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Oral lead-in should be used to assess for tolerability. The most common adverse reactions observed in 2% or more of people receiving Cabenuva in clinical trials were injection site reactions (83%, with 37% having at least Grade 2—moderate), pyrexia (fever), fatigue, headache, musculoskeletal pain, nausea, sleep disorders, dizziness, and rash. Serious post-injection reactions reported within minutes of administration (in less than 1% of people injected) may have been associated with inadvertent (partial) intravenous administration and began to resolve within a few minutes after injection in clinical studies: difficulty breathing (dyspnea), abdominal cramping, agitation, flushing, sweating, oral numbness, and changes in blood pressure. Instructions for injection should be followed carefully to avoid accidental intravenous administration. People given injections should be observed for approximately 10 minutes afterwards to monitor for potential reactions. Liver toxicity (hepatotoxicity) has been reported with or without pre-existing liver disease or risk factors. People with underlying live disease or marked elevations in transaminases (a lab measure that indicates there is damage to the liver) may be at increased risk for rising transaminase level or worsening of current elevated levels. Depressive disorders (including depression, major depression, depressed moods, altered moods, mood swings, dysphoria, negative thoughts, or suicidal ideation and attempts) have been reported with Cabenuva. People experiencing depressive symptoms should be monitored. DHHS guidelines recommend closely monitoring patients with pre-existing psychiatric conditions on an INSTI. Serious or severe hypersensitivity reactions have occurred with other INSTIs and could occur with Cabenuva. Monitor for signs of hypersensitivity, including elevated liver transaminases, and treat as needed. New data associate INSTIs with weight gain; see a different INSTI page for more information. There was a median weight gain of 3.3 pounds in Cabenuva trials.

POTENTIAL DRUG INTERACTIONS

New interactions may be discovered after approval. Cabenuva is contraindicated with carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifabutin, rifampin, rifapentine, systemic dexamethasone (more than one dose), or the herb St. John's wort. Clinical monitoring of methadone is recommended because it may need to be adjusted. 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

As ViiV Healthcare pointed out, Cabenuva changes HIV treatment from 365 dosing days per year to just 12. FDA approval was based on two Phase 3 studies, ATLAS (Antiretroviral Therapy as Long-Acting Suppression) and FLAIR (First Long-Acting Injectable Regimen). See data on the online version of this drug page. Residual concentrations of cabotegravir and rilpivirine may remain in the body for more than a year after discontinuation, but are not expected to affect the use of subsequent HIV drugs.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com; cabenuva.com
(877) 844-8872

AVERAGE WHOLESALE PRICE

28-day oral lead-in provided at no cost
Loading dose (600 mg/900 mg):
$7,128 (estimated based on WAC)
Maintenance dose (400 mg/600 mg):
$4,752/month (estimated based on WAC)

Dr. Melanie Thompson: At long last, Cabenuva was approved by FDA in January, given as two separate injections in the buttock. Thirty days of oral cabotegravir (now called Vocabria) and Edurant will be provided as a lead-in before beginning injectable medicines to ensure viral suppression along with safety and tolerability. After all, once injected, there's no reversing the side effects. In an unusual move, IAS-USA guidelines recommended this combination in advance of FDA approval for the population outlined by FDA. As with Juluca, this regimen should not be used by people with hepatitis B, as neither of the drugs has HBV activity. ATLAS 2M used an 8-week schedule for people who had been on ATLAS, with good result. If FDA approves dosing every 8 weeks, the logistics of administration will be less taxing on patients and clinics—and less expensive! Both drugs last a very long time in the body, in some cases over a year, but the levels decline over time to the point that they won't suppress virus, but could select for resistant virus. Adherence to dosing is therefore very important. These drugs are injected into buttock muscles, not arms. People with buttock implants were excluded from trials. Injection site reactions are common, but tend to be mild and to decrease over time. The prohibition on acid blocking agents with oral rilpivirine does not apply to the injectable form, however, there still can be drug interactions that affect the levels of these and other drugs. Drug interactions should be looked at closely before adding new drugs while taking this regimen.
Implementation will be the challenge for this duo. Dosing will require an increased number of visits for people who are now coming to clinic only every 3 to 6 months or less often. Likewise, reminders will be necessary. This is a great application for smartphone apps, but still requires clinic supervision. For missed injections, additional effort will be needed to help people get to the clinic. This may require transportation support, and visits at non-traditional hours for folks who have difficulty getting off of work. Clearly, administration costs will add to the price of the drugs, and will depend on third-party payors to cover. It is unclear how Ryan White and other public clinics will cover administration costs. These challenges are surmountable, but in the short run it may be difficult to manage this new paradigm as clinics are struggling to manage COVID-19. The annual Wholesale Acquisition Cost for monthly dosing is quite high ($48,720 for the first year) and includes the higher price ($5,940) of the initial loading dose. If injections can be given every 8 weeks, it may lessen the price burden, and become competitive with the also overpriced drugs Biktarvy and Genvoya. (Sorry, here I am on my pricing soapbox again!) Cabenuva won't be for everyone, but some people are eagerly awaiting the opportunity to stop taking pills, even if it means more frequent clinic visits. We need as many options as possible to help people with HIV maintain suppressed virus if we are to end the HIV pandemic.

Activist Bridgette Picou: Cabenuva offers freedom from being tied to daily pills, more privacy about treatment, and less daily effects on the body processes. It's not completely concern free, as the injections have to be given in a healthcare setting, and adherence to the dosing schedule is more important because of its infrequency. A lot of people seem to prefer the idea of monthly injections over daily pills.

Tivicay DTG
dolutegravir

★ Recommended as a component of initial regimen for most people

STANDARD DOSE

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

For adults and children weighing more than 44 pounds (20 kg), use standard dose listed above or see package labeling. New Tivicay PD tablets (5 mg), taken without regard to food, were approved in June and are dispersible in water (oral suspension) for pediatric patients age four weeks and older weighing at least 6.6 pounds (3 kg). Children weighing at least 30.8 pounds (14 kg) may take either Tivicay or Tivicay PD, but Tivicay PD is preferred for those weighing 30.8 up to 44 pounds. Dosing under 44 pounds is weight-based; Tivicay is also available in 10 mg and 25 mg tablets. Do not chew, cut, or crush Tivicay PD tablets. If dose is more than one Tivicay PD tablet, swallow one tablet at a time. If using a dispersible dose, see package insert for mixing instructions. Dosing of Tivicay and Tivicay PD for oral suspension cannot be interchanged on a milligram per milligram basis.

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 observed in 7% of participants in one study. Increased CPK (creatine kinase, a lab value indicating muscle damage), rhabdomyolysis (breakdown of muscle), and myopathy or myositis (muscle pain) were also reported. New data associate INSTIs with weight gain. See weight gain in "More information;" GO TO positivelyaware.com/articles/weighty-concerns and positivelyaware.com/articles/fatty-tissues. There have been rare reports of depression and suicidal ideation, primarily among patients with a history of psychiatric illnesses, in people receiving INSTI-based regimens. 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.

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, Tagamet) and proton pump inhibitors (for example, Aciphex, Dexilant, Prilosec, Prevacid, Protonix, and Nexium) are okay to use. Avoid taking with Viramune, oxcarbazepine, phenytoin, phenobarbital, or St. John's wort. Start metformin at lowest dose and titrate based on tolerability and clinical effect. 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. No known interactions with Epclusa, Harvoni, 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 considered a second-generation INSTI—it may work in many individuals whose virus has developed resistance to other INSTIs, but they will need twice-daily dosing. Compared to other INSTIs, Tivicay has a high genetic barrier against the development of resistance, similar to the protease inhibitors (such as Prezista). Weight gain is becoming more widely recognized as a side effect of INSTIs. In the community, enlargement of the stomach and waist area can be distressing. According to DHHS HIV treatment guidelines, "Weight gain has been associated with initiation of ART [antiretroviral therapy] and subsequent viral suppression. The increase appears to be greater with INSTIs than with other drug classes." Other factors have been associated with weight gain, including race, sex, and previous overweight status. There is no word yet on reversibility, but the race is on to find more answers. Pediatric HIV guidelines include 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.

Another ART (antiretroviral therapy) switch strategy for people who are virally suppressed, backed by some supporting evidence, is moving them 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. Dolutegravir is now a preferred medication at the time of conception as well as during pregnancy, per DHHS perinatal guidelines updated in December. See the online version of this page.

Dr. Melanie Thompson: Dolutegravir is recommended as a first-line option for initial treatment, in combination with TDF or TAF, and FTC or 3TC. It also can be taken with ABC/3TC, or with 3TC alone in STR formulations.

Resistance to dolutegravir can occur but is less common than to raltegravir and elvitegravir.

Weight gain was higher with dolutegravir than raltegravir in the large NA-ACCORD cohort study, and higher than with elvitegravir/cobicistat in a pooled analysis.

Early data from the Tsempano study in Botswana suggested that persons on dolutegravir at the time they became pregnant were more likely to have infants with neural tube defects (birth defects affecting the developing nervous system) than those not taking dolutegravir at conception. Based on that, dolutegravir-containing regimens were recommended as alternatives for persons planning pregnancy or those not using adequate contraception. Updated data, however, now show only a very small increase in risk for neural tube defects in those on dolutegravir at the time of conception, suggesting that the benefits of improved viral suppression on dolutegravir may outweigh the risks. While the risk is small, providers should discuss with people capable of pregnancy before starting dolutegravir. There have been no concerns about using dolutegravir in the second or third trimesters of pregnancy.

There are fewer drug interactions with dolutegravir than with boosted drugs, but several are notable. Dofetilide, a heart rhythm medication, should never be taken with dolutegravir. Dolutegravir can increase levels of metformin, and levels of dolutegravir are decreased by etravirine and efavirenz when no booster is present. Calcium, magnesium, zinc, aluminum, and iron supplements can lower INSTI levels and dosing recommendations should be observed.

Activist Bridgette Picou: Tivicay is to be used as part of an HIV cocktail or regimen. Side effects may include headache and diarrhea. It can be taken with or without food, and is dosed as once a day, or twice a day if there is resistance to other intergrase inhibitors.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

50 mg tablets: **$2,300.04**/month

Isentress HD (and Isentress) RAL raltegravir

★ Recommended as a 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 containing 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 an oral suspension and flavored chewable tablets. Isentress dosing is based on weight for children less than 55 pounds; 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. See weight gain in "More information;" GO TO positivelyaware.com/articles/weighty-concerns and positivelyaware.com/articles/fatty-tissues. 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. INSTIs have been associated with adverse neuropsychiatric effects in some retrospective cohort studies and case series. 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

It is important to take Isentress HD and Isentress only with other HIV drugs recommended by your provider because they and similar drugs are contained in other HIV medications: Biktarvy, Genvoya, Stribild, Tivicay, Triumeq, Dovato, and Juluca. Isentress HD cannot be used with rifampin, but Isentress can; increase Isentress to 800 mg twice daily when using 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 Harvoni, 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 not listed here.

MORE INFORMATION

Isentress HD was approved in 2017. While the original formulation, Isentress, was well tolerated and highly effective, its twice-daily dose was seen by some as a small inconvenience. According to DHHS HIV treatment guidelines, most INSTIs on the market are recommended as components of initial ART regimens for most people; Isentress HD has been added to this list. Raltegravir-based regimens may be preferred for patients with high cardiovascular risk. Weight gain is being more commonly recognized as a side effect of INSTIs. In the community, enlargement of the stomach and waist area can be distressing. According to the DHHS HIV treatment guidelines, "Weight gain has been associated with initiation of ART [antiretroviral therapy] and subsequent viral suppression. The increase appears to be greater with INSTIs than with other drug classes. Greater weight increase has also been reported with TAF than with TDF, and greater with DOR than EFV." Other factors have been associated with weight gain in addition to medication used, including race, sex, and previous overweight status. There is no word yet on reversibility, but the race is on to find more answers. 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 for children ages 6–12.

Dr. Melanie Thompson: Raltegravir comes in a one pill, twice daily formulation, and a two pill, once daily formulation (HD.) It was the first INSTI and now is the only INSTI not available in an STR formulation.

Isentress has a lower barrier to resistance than dolutegravir or bictegravir, or boosted PIs. Dolutegravir and bictegravir are preferred for rapid ART start, due to their high barrier to resistance. Isentress was a revolutionary drug in its moment, but it has become a lesser used INSTI due to genetic fragility, pill burden, and lack of an STR formulation.

Isentress has been associated with more weight gain than boosted atazanavir, darunavir, or elvitegravir, but less than dolutegravir.

Calcium, magnesium, zinc, aluminum, and iron supplements can lower levels of INSTIs and dosing recommendations should be observed.

Activist Bridgette Picou: Isentress HD and Isentress are integrase inhibitors. The generic name is raltegravir. They can be used for treatment-naïve persons, as well as treatment-experienced individuals who have multi-drug resistance and have not taken an integrase inhibitor before. Dosing for Isentress HD (600 mg) is two pills once a day, and for Isentress (400 mg) one pill twice a day. Other uses include being part of a PEP (post-exposure prophylaxis) treatment and as an oral or chewable tablet for children. If you develop a rash from Isentress, discontinue use and contact your clinician.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

Isentress HD 600 mg, 60 tablets:
$2,082.24/month
Isentress 100 mg, 60 chewables:
$520.56/month
Isentress 100 mg, 60 packets:
$520.56/month
Isentress 400 mg, 60 tablets:
$2,082.24/month

Prezcobix

DRV/COBI
darunavir/cobicistat

✔ Recommended as a 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.

Prezcobix is for adults and children weighing at least 88 pounds (40 kg). Prezcobix is only available for people taking darunavir once daily, not those who require darunavir twice daily (see Prezista). 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). See "More information" for CrCl information.

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. 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

Darunavir (which is in Prezcobix) contains a sulfa component, and should be taken with caution by people with a known sulfonamide allergy. The most common side effects reported in at least moderate severity by 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 of 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. While very rare (0.4% incidence), severe rash accompanied in some cases by fever and/or elevations of AST/ALT (liver enzymes), can be life-threatening. Seek immediate medical attention. Observational cohort studies reported an association between some PIs (including darunavir taken with Norvir) and an increased risk of cardiovascular (CV) events. Data with darunavir plus cobicistat are too limited to make these conclusions. Although some older PIs have been associated with liver toxicity, lactic acidosis, diabetes, or fat redistribution, these conditions are only rarely, or never, observed with darunavir. With PIs, there can be increased risk for bleeding in hemophiliacs.

POTENTIAL DRUG INTERACTIONS

Cobicistat interacts with many drugs because, as a booster, it inhibits liver enzymes involved in drug metabolism. Note: cobicistat is not interchangeable with ritonavir; however, drug interactions with Prezcobix are very similar to Prezista + Norvir. See those individual pages for more information. Do not take with betamethasone, budesonide, carbamazepine, ciclesonide, dexamethasone, dronedarone, ergot derivatives, eslicarbazepine, fluticasone, ivabradine, triazolam, oral midazolam, lomitapide, lurasidone, methylprednisolone, mometasone, naloxegol, 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 (Eliquis) dose may need to be adjusted. Beclomethasone, prednisolone, and prednisone as alternative corticosteroids may be considered, particularly for long-term use. Erectile dysfunction drugs should not exceed 10 mg Cialis, or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours. Atorvastatin and rosuvastatin dose should not exceed 20 mg daily. Clinical monitoring is recommended with drospirenone, due to potential for hyperkalemia (higher than normal potassium level in your blood). Do not take with colchicine if there is kidney or liver impairment. Start metformin at lowest dose and titrate based on tolerability and clinical effect. Cannot be taken with Zepatier. Not recommended with Mavyret. Based on its mechanism, drug interactions with other hepatitis C medications are similar to the interactions of 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 pharmacokinetic (PK) enhancer or booster 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. A single-tablet, once-daily regimen containing darunavir/COBI/FTC/TAF is 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 hivinfo.nih.gov]." Examples of people needing to start treatment immediately before resistance test results are available include newly diagnosed individuals and those who are experiencing certain opportunistic infections (an indication of advanced disease). Doctors regularly prescribe Prezcobix for patients with a CrCL less than 30 mL/min and for patients on dialysis, although the label has not been updated with new data after Prezcobix came to market. There are no pharmacokinetic data available with Prezcobix in renal impairment or end-stage renal disease.

Dr. Melanie Thompson: Darunavir/cobicistat and Evotaz were the first coformulated boosted PIs to hit the market since Kaletra. It is recommended for initial treatment when INSTIs can't be used, and can be paired with TAF/FTC, TDF/FTC, and ABC/3TC.

For side effects and drug interactions, see also Prezista and Tybost.

Prezcobix should not be used during pregnancy because of insufficient drug levels associated with cobicistat.

Activist Bridgette Picou: Prezcobix needs to be taken as part of a cocktail ART regimen with other HIV medications. Take once daily with food, and try not to skip doses. Prezcobix does, however, have a high barrier to resistance should there be doses missed. Other drugs can affect the metabolism of Prezcobix, so discuss all medications taken with your clinician.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$2,530.82/month

Prezista

DRV
darunavir

✔ Recommended as a component of initial regimen in certain clinical situations

STANDARD DOSE

One 800 mg tablet plus 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. Suspension should be shaken before each use and stored at room temperature. Do not refrigerate.

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 by patients with known sulfonamide allergy. 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 people with severe liver impairment. While very rare, severe rash can be accompanied by fever and/or elevations of liver enzymes, and can be life-threatening. Seek immediate medical attention. When used with Tybost a small increase in serum creatinine (SCr) may be observed that does not translate to a decrease in kidney function. Observational cohort studies reported an association between some PIs (including darunavir taken with ritonavir) and an increased risk of cardiovascular events. Although some older PIs have been associated with liver toxicity, lactic acidosis, diabetes, or fat redistribution, these conditions are only rarely—if at all—observed 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 risk for bleeding in hemophiliacs.

POTENTIAL DRUG INTERACTIONS

Drug interactions of Prezista + Norvir may be different from those with Prezista + Tybost. Note: Tybost is not interchangeable with Norvir. Do not take with alfuzosin, cisapride, colchicine (in patients with kidney or liver impairment), dronedarone, ivabradine, lomitapide, lurasidone, naloxegol, ranolazine, pimozide, ergot derivatives, triazolam, oral midazolam, rifampin, Revatio, St. John's wort, or Zepatier. Not recommended with the blood thinners everolimus, rivaroxaban (Xarelto), or ticagrelor. Not recommended with Mavyret (glecaprevir/pibrentasvir), simeprevir, rifapentine, irinotecan, salmeterol, and avanafil. 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, phenytoin, and phenobarbital is recommended. Reducing 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 75% in kidney impairment. The antifungal drugs isavuconazole, posaconazole, ketoconazole, and itraconazole should be used with caution (maximum dose is 200 mg per day for the last two). 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 corticosteroids may be considered, particularly for long-term use. Erectile dysfunction drugs should not exceed 10 mg Cialis, or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours. Effectiveness of oral contraceptives may be decreased; consider using alternative methods of contraception. Monitoring is recommended for co-administration with drospirenone due to the potential for hyperkalemia (higher than normal potassium levels in the blood). Monitoring is recommended with buprenorphine, buprenorphine/naloxone, and 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, propafenone, and quinidine. Cannot be taken with Zepatier. Based on its 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, as there are many other drug interactions not listed here.

Dr. Melanie Thompson: Darunavir quickly became the "go to" PI because of its tolerability, hardy activity against resistant virus, and once daily dosing (at 800 mg) with a booster when viral resistance is not a concern. It should be taken twice daily at 600 mg with a booster in the setting of resistance. It is available coformulated with cobicistat as Prezcobix, and with cobi, TAF, and FTC as Symtuza.

Darunavir may cause an allergic reaction in some, but not all, people who are allergic to sulfa. Boosted darunavir has many drug interactions due to the booster, but also due to its own pharmacologic properties that raises some drug levels and lowers others. Don't guess about this—look it up and consult an expert! This is one reason that boosted drugs are no longer considered first choice for therapy. Large cohort studies have associated darunavir, like abacavir, with increased rates of cardiovascular disease.

Activist Bridgette Picou: Like other boosted regimens, Prezista is metabolized in the liver, which means potential drug-drug reactions. Discuss all supplements and over-the-counter medications with your provider. An advantage could be that it is lipid friendly. Side effects can happen and should be discussed with a clinician to see if there are other more tolerable options.

MORE INFORMATION

Prezista 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." Examples of people needing to start treatment immediately before resistance test results are available include newly diagnosed individuals, pregnant women, and those who are experiencing certain opportunistic infections (an indication of advanced disease). Read about regimens in the online version of this page. Prezista + Norvir is a preferred component in the DHHS perinatal guidelines for use in pregnancy.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

600 mg, 60 tablets: **$2,214.23**/month
800 mg, 30 tablets: **$2,214.23**/month

Evotaz

ATV/COBI
atazanavir/cobicistat

✔ Recommended as a 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. See "More information" for pediatric dose update.

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, Temixys, 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 (TAF, found in Biktarvy, Descovy, Genvoya, Odefsey, and Symtuza, and under the brnad name Vemlidy) is not recommended if kidney function as measured by creatinine clearance is below 30 mL/min.

Not recommended for 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.

➤ 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. The ocular icterus and jaundice were reversible on discontinuation of the drug. 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. Note—Tybost is not interchangeable with Norvir. 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. Proton pump inhibitors (PPIs, like Aciphex, Dexilant, Nexium, Prilosec, Protonix, and Prevacid) and H2-receptor antagonists (H2RAs, like Pepcid, Zantac, and Tagamet) can stop atazanavir from being absorbed. Treatment-experienced people should not take PPIs while on atazanavir. See package insert for antacid dosing adjustment recommendations. If taking chewable antacids such as Rolaids and Tums, take atazanavir with food two hours before or one hour after. Monitoring is required when used with warfarin. Calcium channel blockers should be monitored. Reducing dose and frequency of rifabutin to 150 mg every other day or three times a week is recommended. Evotaz increases levels of fluticasone (found in Advair, Arnuity Ellipta, Breo Ellipta, Flonase, and Flovent); monitor for signs of Cushing's syndrome (increased abdominal fat, fatty hump between the shoulders, rounded face, red/purple stretch marks, bone loss, increased appetite, possible high blood pressure, and sometimes diabetes). An alternative corticosteroid is recommended. Erectile dysfunction 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. Start metformin at lowest dose and titrate based on tolerability and clinical effect. 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.

Dr. Melanie Thompson: The second dual PI coformulation with cobicistat, Evotaz is infrequently used because of its many drug interactions and side effects. (See Reyataz and Tybost.)

It can be used for treatment with one of the tenofovir-containing nuke backbones, but it is generally now prescribed mainly for people who have been on long-term atazanavir with good results who wish to maintain this regimen.

It is not recommended in pregnancy because of insufficient drug levels associated with cobicistat.

Activist Bridgette Picou: Evotaz consists of an HIV medication and a booster. It is not a full regimen on its own. The absorption of atazanavir can be affected by medications taken for heartburn, so you need to make your clinician aware if you take those. The cobicistat means drug-drug interactions with other medications are also possible. Evotaz can be used in both treatment-naïve and treatment-experienced patients.

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 such as 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 compared to other regimens in this category. In October 2019, the FDA approved a pediatric dose for Tybost (the brand name for cobicistat). The approval also allowed Tybost and Reyataz to be taken by pediatric patients weighing at least 77 pounds (35 kg). (Reyataz was already approved for pediatric use.) Although the Evotaz label was not changed to note this approval, it is presumed that pediatric patients weighing at least 77 pounds can take Evotaz.

MANUFACTURER

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

AVERAGE WHOLESALE COST

$1,926.56/month

GENERIC IS AVAILABLE

Reyataz

atazanavir, or ATV
atazanavir sulfate

✔ Recommended as a 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 eyes as a result of increased bilirubin levels), jaundice, and rash. The ocular icterus and jaundice are reversible upon 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 on all patients before starting 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.

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). 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

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. Note: Tybost is not interchangeable with Norvir. Proton pump inhibitors (PPIs, like Aciphex, Dexilant, Nexium, Prilosec, Protonix, and Prevacid) and H2-receptor antagonists (H2RAs, like Pepcid, Zantac, and Tagamet) can prevent Reyataz from being absorbed. Treatment-experienced people should not take PPIs while on Reyataz. See package insert for antacid dosing adjustment recommendations. If taking chewable antacids such as 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 levels of Reyataz, and Reyataz/Norvir increases Viread levels; monitor for adverse events. Reyataz can be taken unboosted with Epzicom if absolutely necessary (Reyataz dose of 400 mg daily). Bepridil, amiodarone, quinidine, and lidocaine should be taken with caution because of the risk for 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, Breo Ellipta, Arnuity Ellipta, Flonase, and Flovent); monitor for signs of Cushing's syndrome (increased abdominal fat, fatty hump between the shoulders, rounded face, red/purple stretch marks, bone loss, increased appetite, possible high blood pressure, and sometimes diabetes). 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. Erectile dysfunction 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. Reyataz/Norvir is not recommended with Harvoni if tenofovir DF (TDF, in Truvada) is part of an HIV regimen. With Epclusa, monitor for tenofovir toxicities if TDF is part of an HIV 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 many other drug interactions not listed here.

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 (co-formulated as Evotaz) 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 compared to other regimens in this category.

Dr. Melanie Thompson: Atazanavir became popular because it was once daily, lipid-neutral, and more tolerable than first generation PIs. It is approved unboosted at a high dose, but it is recommended only when used with ritonavir or cobicistat. It is no longer a first-line agent because of its substantial side effects, including jaundice, gallstones, and kidney stones, as well as many drug interactions associated not only with boosters, but also with the drug itself. In fact, it's unclear that atazanavir plays any role at all in the landscape of current therapy.

Reyataz should not be paired with ABC/3TC due to higher risk of virologic failure.

Acid-blocking medications lower the absorption of atazanavir, and should be avoided.

Atazanavir has not been associated with increased rates of cardiovascular disease in large cohort studies.

Activist Bridgette Picou: When taking Reyataz you may notice yellowing of the skin and eyes. This usually reverses once the medication is stopped and is a result of bilirubin. Monitor the kidneys and liver. While drug-drug interactions, such as with antacids, should be monitored, Reyataz is lipid friendly.

MANUFACTURER

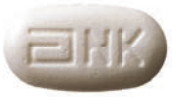
Bristol-Myers Squibb
reyataz.com; (800) 321-1335

AVERAGE WHOLESALE PRICE

50 mg, 30 packets: **$271.22**/month
150 mg, 60 capsules: **$1,755.91**/month
300 mg, 30 capsules: **$1,739.30**/month

Generic atazanavir
150 mg, 60 capsules: **$1,668.11**/month
300 mg, 30 capsules: **$1,652.34**/month

PKE | **Pharmacokinetic enhancer (booster);** also an antiretroviral (protease inhibitor)



GENERIC IS AVAILABLE

Norvir

RTV
ritonavir

✔ Used only as a booster for other drugs; recommended as a component of initial regimen in certain clinical situations

STANDARD DOSE

Used as a boosting agent (or PK enhancer) 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 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. The liquid formulation 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 formulation), 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. Of note, Norvir is not interchangeable with Tybost. Also, Norvir tablets are not interchangeable with Norvir capsules. 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, increased appetite, 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. Taking Norvir with most other blood thinners (anticoagulants), such as Xarelto, is not recommended; however, it can be used with apixaban (Eliquis) with monitoring and an adjusted dose of apixaban. 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 four 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 a 2–3-fold increase in methamphetamine concentrations, increasing the risk for overdose. GHB, another street drug, as well as cocaine are 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 many other drug interactions which are not listed here.

MORE INFORMATION

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

Dr. Melanie Thompson: One of the first HIV protease inhibitors, ritonavir is now rarely used, and only to boost the protease inhibitors atazanavir or darunavir. This boosting effect also causes multiple drug interactions with many other drugs, raising levels of some and lowering others, so it is important to check out each medication separately for drug interactions.

Because Abbott would not allow ritonavir to be coformulated with any other than its own drugs, there were no coformulated PIs, except Kaletra, until cobicistat came around. Ritonavir has been largely supplanted by cobicistat because it allows coformulation.

The drug interactions of ritonavir and cobicistat are slightly different, so before changing from one to the other, review interactions for each coadministered drug carefully.

Ritonavir became generic in 2018. Like most HIV generics, by the time it is off patent, it's just not used any more. Could we look at those patent laws, please?

Activist Bridgette Picou: Norvir is no longer used as a frontline medication, but in lower doses is still an effective booster for other HIV medications, specifically protease inhibitors. Norvir will increase the effects of these and other medications.

MANUFACTURER

AbbVie
norvir.com; (800) 633-9110

AVERAGE WHOLESALE PRICE

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

Tybost

COBI
cobicistat

✔ Used only as a booster for other drugs; recommended as a component of initial regimen in certain clinical situations

STANDARD DOSE

Used as a boosting agent (or PK enhancer) at a dose of 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, Genvoya, and Symtuza.

For adults and children weighing at least 77 pounds (if taken with atazanavir, brand name Reyataz) or at least 88 pounds (if taken with darunavir, brand name Prezista or in the single-tablet regimen Symtuza; darunavir patients must be at least three years old). 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 rash, 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 (SCr), 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-administration of Tybost and Viread (tenofovir DF or TDF, also found in Cimduo, Complera, Delstrigo, Symfi/Symfi Lo, Stribild, Truvada, and Temixys) 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, increased appetite, 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. Start metformin at lowest dose and titrate based on tolerability and clinical effect. 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, also the single-tablet regimen Symtuza). Cobicistat is also part of the single-tablet regimens Genvoya and Stribild to boost the elvitegravir component. All of these aforementioned regimens are recommended in the DHHS treatment guidelines for use 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 elvitegravir, darunavir, or atazanavir should not be initiated in pregnant individuals and is not recommended during pregnancy. Inadequate levels of ART (antiretroviral therapy) in second and third trimesters as well as viral breakthroughs have been reported. Tybost is not recommended during pregnancy.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$304.00/month

Dr. Melanie Thompson: Cobicistat is now the most commonly used booster, and because it can be coformulated, it is rarely used as a separate pill. Unlike ritonavir, cobicistat has no activity against HIV.

Cobicistat has many drug interactions, but it has a slightly different drug interaction profile compared with ritonavir, and these interactions must be managed carefully. Because cobicistat and ritonavir are not exactly interchangeable, it is important to be very careful when changing from one to the other. Consult an expert if there are any doubts about drug interactions!

Activist Bridgette Picou: Think of Tybost as just what the name implies, a booster. It is not an antiretroviral itself, but it works with other HIV drugs to increase effectiveness. As a pharmacokinetic enhancer, the mechanism of action is in the liver, which means monitoring for drug-drug reactions. You should also monitor your lipids and triglycerides. Watching your diet and food intake may help with this.

Descovy

FTC/TAF
emtricitabine/tenofovir alafenamide

★ Recommended as a 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 (TAF). For adults and children weighing at least 55 pounds (25 kg), or 77 pounds (35 kg) if taking Descovy with a boosted protease inhibitor. Must be taken in combination with another antiretroviral(s) that does not contain the medications in this drug combination.

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's prescribing information indicates that it should not be used if CrCl is less than 30 mL/min, but data have shown that it can be used safely in patients with end stage renal disease on hemodialysis and with CrCl less than 15 mL/min. Descovy was approved for HIV prevention (pre-exposure prophylaxis, or PrEP) in October 2019; see "Descovy for PrEP" page.

- **SEE THE INDIVIDUAL DRUGS CONTAINED IN DESCOVY:** Emtriva (TAF is not available separately for HIV, but is used to treat hepatitis B under the brand name Vemlidy).
- **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 people may experience nausea, headache, stomach pain, or changes in weight. New data associate INSTIs and TAF with potential weight gain; see "More information," and **GO TO** positivelyaware.com/articles/weighty-concerns and positivelyaware.com/articles/fatty-tissues. 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 bone or kidney problems. Prior to initiation, people should be tested for hepatitis B virus (HBV) infection. Severe exacerbations of hepatitis B have been reported in people co-infected with hepatitis B who have discontinued Descovy (due to elimination of both emtricitabine and TAF, which also treat HBV). Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted upon Descovy discontinuation. Call your health care provider right away if you develop any of the following signs or symptoms of hepatitis: 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.

POTENTIAL DRUG INTERACTIONS

Do not take with Cimduo or Temixys, Emtriva, Epivir-HBV, Hepsera, Truvada, Viread, 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 such as 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, 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 similar to Truvada, except that instead of TDF, Descovy contains TAF (tenofovir alafenamide), which reduces serum tenofovir concentration by up to 90%. This results in a decreased impact on kidney and bone demineralization but maintains potent antiviral activity in the CD4 cell. In clinical trials, fewer kidney and bone issues were observed with TAF than with TDF, and significant improvements were observed 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, and in fact one or the other combination is found in some of the single-tablet regimens. Weight gain is being more commonly recognized as a potential side effect of TAF. In the community, enlargement of the stomach and waist area can be distressing. According to the DHHS HIV treatment guidelines, "Weight gain has been associated with initiation of ART [antiretroviral therapy] and subsequent viral suppression. The increase appears to be greater with INSTIs than with other drug classes. Greater weight increase has also been reported with TAF than with TDF, and greater with DOR than EFV." Other factors have been associated with weight gain in addition to medication used, including race, sex, and previous overweight status. There is no word yet on reversibility, but the race is on to find more answers. Descovy received FDA approval in October 2019 for the prevention of sexually acquired HIV (pre-exposure prophylaxis, or PrEP) in adults and adolescents weighing at least 77 pounds, excluding individuals at risk from receptive vaginal sex due to a lack of data in this population. It was studied in men who have sex with men and transgender women; other studies are ongoing. See Descovy for PrEP page. 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 recommend Descovy as part of a preferred regimen. TAF is now an alternative NRTI for use in pregnancy, according to DHHS perinatal guidelines updated in December. Descovy tablets are relatively small compared to Truvada and other combination tablets, which may be helpful to patients who have difficulty swallowing.

Dr. Melanie Thompson: Coformulated tenofovir alafenamide and emtricitabine (TAF/FTC) is edging out TDF/FTC as the most popular nuke backbone because TAF has higher tenofovir levels in cells and lower levels in blood, resulting in less effect on kidneys and bone than TDF. Therefore, TAF is safe to use by people whose kidney function is somewhat impaired (estimated glomerular filtration rate equal to or greater than 30 mL/min).

Several recent developments may slow the trend toward TAF. Recent studies indicate that TAF may result in more weight gain than TDF, especially with INSTIs. Both HDL and LDL cholesterol levels are higher with TAF than TDF, although the HDL total cholesterol ratio remains unchanged, so the significance is not entirely clear. Finally, the approval of generic coformulations of TDF/3TC and TDF/FTC may offer a (somewhat) cheaper dual-nuke alternative for those able to take TDF.

Activist Bridgette Picou: By now many people both HIV positive and negative have heard of "the little blue pill." Descovy is the reformulation of Truvada. Tenofovir alafenamide fumarate replaces the tenofovir disoproxil in the original formulation. The alafenamide means less medication, and therefore lessened side effects on the body, namely kidney toxicity and bone density issues. Descovy is found in some of the newer STRs as well as fixed-dose tabs, and is also used for PrEP (see Descovy for PrEP).

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$2,316.85/month

GENERIC IS AVAILABLE

Truvada

FTC/TDF
emtricitabine/tenofovir disoproxil fumarate

★ Recommended as a 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 (35 kg). In children weighing 37–76 pounds (17–34 kg), Truvada is dosed based on body weight. See package insert for weight-based dosing. Truvada tablets are available in the following emtricitabine/tenofovir DF (TDF) dosages: 100/150 mg tablets, 133/200 mg tablets, 167/250 mg tablets, and 200/300 mg tablets. Tablets can dissolve 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. When used for HIV treatment, Truvada must be taken in combination with another antiretroviral(s) that does not contain the medications in this drug combination.

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 who have 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 30 mL/min (less than 60 mL/min if used for PrEP) or if you are on dialysis. Truvada was approved for HIV prevention (pre-exposure prophylaxis, or PrEP) in 2012; see "Truvada for PrEP" page.

➤ **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

Overall, Truvada is well tolerated, but some people may experience nausea, headache, bloating, 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 for 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 bone or 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. Prior to initiation, people should be tested for hepatitis B virus (HBV) infection. Severe exacerbations of hepatitis B have been reported in people co-infected with hepatitis B who have discontinued Truvada (due to elimination of both emtricitabine and TDF, which also treat HBV). Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted upon Truvada discontinuation. Call your health care provider right away if you develop any of the following signs or symptoms of hepatitis: 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. Truvada is associated with lower lipid levels than Ziagen or TAF due to TDF's favorable effect on LDL (bad) cholesterol (although it also lowers levels of HDL, or good cholesterol). The ratio of total cholesterol to HDL remains the same as that of TAF. Truvada contains lactose, which can cause some abdominal discomfort, especially in patients sensitive to lactose. See weight discussion in the online version of this page.

POTENTIAL DRUG INTERACTIONS

Do not take with Cimduo or Temixys, Descovy, Emtriva, Epivir-HBV, Hepsera, Vemlidy, or Viread, all used for the treatment of hepatitis B. Tenofovir DF decreases the concentration levels of Reyataz, therefore when Reyataz is taken with Truvada or Viread, it is recommended that Reyataz 300 mg be 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 DF concentrations. It is recommended that people 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 such as Advil or Motrin (ibuprofen) and Aleve (naproxen). Truvada may be used with hepatitis C drugs Harvoni 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 interactions not listed here.

MORE INFORMATION

Don't believe the lawsuit advertisers: Truvada is a safe medication to take. As with any drug therapy, some people will experience side effects. Adverse events are rare and usually reversible. See "Truvada Safety" in the September+October 2019 issue of POSITIVELY AWARE (positivelyaware.com/articles/truvada-safety). 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 ACTG A5202 study reported that while both Epzicom and Truvada reduced viral load, for 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 among 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 people who have underlying kidney problems or are at higher risk for them. Fewer kidney and bone issues were observed with the TAF formulation compared to TDF in clinical trials. Truvada is approved for HIV prevention; see Truvada for PrEP page. Truvada is recommended by DHHS as one of the preferred NRTI combination components of an ART regimen in pregnancy. Truvada generic became available in the U.S. in October 2020. See discussion of the generic's pricing in the January+February 2021 issue.

Dr. Melanie Thompson: Coformulated tenofovir disoproxil fumarate and emtricitabine (TDF/FTC) is a potent and durable backbone that can be used with all INSTIs, NNRTIs, and boosted PIs for treatment and, as a standalone, for prevention. (See Truvada for PrEP.)

Both TDF and FTC have activity against hepatitis B and stopping the drug can cause a flair of hepatitis B.

TDF can cause kidney dysfunction as well as decreases in bone density over time. This is especially of concern for older people, or people who have other conditions such as diabetes or hypertension that can affect kidney function. Likewise, it could be of concern for menopausal women in whom bone density commonly declines. However, TDF/FTC remains a good choice for younger people without a lot of other medical conditions who have good kidney function (and probably bone density) before starting TDF/FTC.

Because ritonavir and cobicistat boosters also raise blood levels of TDF, the "bystander" toxicity of TDF to kidneys and bone appear to be worse with boosters, and this should be considered for people who already have kidney or bone problems or who are at high risk.

Generic TDF/FTC is made by Teva but the cost is disappointingly high, at $48.51 per tablet. Do not ever think that generic is synonymous with inexpensive, as once was the case. Teva offers a co-pay card to offset $600/month of out-of-pocket costs.

Activist Bridgette Picou: In recent years Truvada became better known for its use as PrEP (see Truvada for PrEP) than as part of an HIV therapy, but it is used for both. Both can affect bone health and the kidneys. You should be monitored regularly for these if you are prescribed Truvada.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$2,210.74/month
generic: **$2,100.20**/month

Cimduo and Temixys

3TC/TDF
lamivudine/
tenofovir DF

★ Recommended as a 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 (35 kg). Tablet contains 300 mg lamivudine (3TC) and 300 mg tenofovir disoproxil fumarate (TDF). Must be taken in combination with another antiretroviral(s) that does not contain the medications (or their equivalents) in this drug combination.

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 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). TDF 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 bone or 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. Prior to initiation, people should be tested for hepatitis B virus (HBV) infection. Severe exacerbations of hepatitis B have been reported in people co-infected with hepatitis B who have discontinued medication (due to elimination of both lamivudine and TDF, which also treat HBV). Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted upon discontinuation. Call your health care provider right away if you develop any of the following signs or symptoms of hepatitis: 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. Contains lactose, which can cause some abdominal discomfort, especially in patients sensitive to lactose. Read weight discussion in the online version of this page.

POTENTIAL DRUG INTERACTIONS

Do not take with Descovy, Emtriva, Epivir-HBV, Hepsera, Truvada, Vemlidy, or Viread, which are used for the treatment of hepatitis B. Tenofovir DF decreases the concentration levels of Reyataz, therefore when Reyataz is taken with Cimduo or Temixys, it is recommended that Reyataz 300 mg be taken with Norvir 100 mg (all as a single daily dose with food). In addition, Reyataz/Norvir, Prezista/Norvir, and Kaletra increase tenofovir DF concentrations; therefore, it is recommended patients be monitored for TDF-associated adverse events, particularly decreases in kidney function. Avoid taking with drugs that negatively affect the kidneys, including chronic use or high doses of anti-inflammatory drugs for pain such as 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 hepatitis C (HCV) treatment. (Of note, interferon alfa is no longer used for the treatment of hepatitis C). Cimduo and Temixys may be used with HCV drugs Harvoni 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 interactions not listed here.

MORE INFORMATION

Cimduo and Temixys are slightly different versions of Truvada, but contain 3TC instead of Truvada's FTC. The two meds are essentially equivalent. The niche for these medications is that they may be a cheaper option for some insurance plans because they contain generic drugs. They also allow for some new or unique co-formulations (such as with Delstrigo, Symfi, and Symfi Lo). Cimduo and Temixys received DHHS HIV treatment guidelines recommendation as a component for initial ART for most people with HIV. TDF is falling out of favor since the newer formulation tenofovir alafenamide (TAF) was approved. TAF is safer on kidneys and bones than TDF. Unlike Truvada, Cimduo and Temixys are not approved for PrEP (HIV prevention). DHHS treatment guidelines recommend Cimduo, Temixys, 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 and these 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 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 and Temixys are recommended by DHHS as one of the preferred NRTI combination components of an ART regimen during pregnancy.

Dr. Melanie Thompson: Because tenofovir disoproxil fumarate (TDF) and lamivudine (3TC) are both off-patent, new combination tablets are now available. Coformulated TDF/3TC is accepted by guidelines panels as interchangeable with TDF/FTC for treatment (but not prevention!) and is recommended as a nuke backbone option for starting treatment.

Both TDF and 3TC have activity against hepatitis B.

Although this is confusing, these combination tablets are technically "brand"—not generic—drugs, even though both components are off-patent. This means that, unlike for generic drugs, the manufacturers can provide co-pay cards/coupons that cover some out-of-pocket costs, just as happens for other brand-name HIV drugs.

Now, here's my editorial comment about all of this. It is extremely disappointing that the price of these drugs is still high, with a Wholesale Acquisition Cost (WAC) of $10,000–12,000. They are relatively cheap to make, and the manufacturers, Mylan and Celltrion, didn't have to do the research to develop them. There are co-pay cards to offset some out-of-pocket costs, but allow the manufacturer to maintain high prices.

Activist Bridgette Picou: Both medications are fixed-dose combination pills containing two medications, lamivudine and tenofovir DF (TDF). As used in daily dosing, you can take them with or without food. Because of the TDF component, you will need to test for kidney toxicity and bone health. Know your hepatitis B virus (HBV) status. Do not suddenly stop these medications if you have HBV, as it can cause a harmful flare up of your hepatitis. Both are lower-cost alternatives taken in conjunction with other HIV meds to complete a regimen.

MANUFACTURERS

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

Celltrion, Inc.
celltrion.com; temixys.com;
contact@celltrion.com

AVERAGE WHOLESALE PRICE

Cimduo: **$1,206.56**/month
Temixys: **$1,020.00**/month

GENERIC IS AVAILABLE

Epzicom

ABC/3TC
abacavir/lamivudine

★ Recommended as a 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 combination.

Approved for adults and children weighing 55 pounds (25 kg) or more. 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. According to the drug label, Epzicom is not recommended for people with decreased kidney function (creatinine clearance less than 50 mL/min) due to lamivudine component, or those with moderate or severe liver impairment due to abacavir component. This medication combination, however, is often used in reduced renal function below 50 mL/min, due to relatively minimal risk of lamivudine accumulation and side effects. In addition, alternative doses may be obtained by using the individual components of this medication as needed.

- 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

Common side effects may include headache, nausea, fatigue, depressed mood, dizziness, diarrhea, rash, or 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 simple blood test for HLA-B*5701 (a genetic marker) should be done before starting an HIV regimen containing abacavir to identify people 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% or less from clinical studies. This test is covered by most insurances and also by LabCorp/ViiV (see company contact on co-pay chart).

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 smoking, diabetes, uncontrolled 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 absolute 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.

Prior to initiation, people should be tested for hepatitis B virus (HBV) infection. Severe exacerbations of hepatitis B have been reported in people co-infected with hepatitis B who have discontinued Epzicom (due to elimination of the lamivudine component, which also treats HBV). Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted upon Epzicom discontinuation. Call your health care provider right away if you develop any of the following signs or symptoms of hepatitis: 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.

POTENTIAL DRUG INTERACTIONS

See the individual drugs contained in Epzicom—Epivir and Ziagen. It is important to take Epzicom only with other HIV medications recommended by your provider because Epzicom and its equivalent drugs are contained in other HIV medications: Atripla, Biktarvy, Cimduo, Combivir, Complera, Delstrigo, Descovy, Dovato, Emtriva, Epivir, Genvoya, Odefsey, Stribild, Symfi, Symfi Lo, Symtuza, Temixys, Triumeq, Trizivir, Truvada, or Ziagen; also 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 the hepatitis C drugs Epclusa, Harvoni, or Zepatier, depending on the third drug in the HIV regimen. 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 for 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 abacavir/lamivudine (Epzicom) was inferior to tenofovir/emtricitabine (Truvada) in getting people undetectable when their pre-treatment viral load was above 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 hepatitis B virus; see Epivir. Epzicom is recommended by DHHS as one of the preferred NRTI combination components of an ART regimen in pregnancy.

Dr. Melanie Thompson: Abacavir/lamivudine (ABC/3TC) is recommended for initial therapy in most persons only in combination with dolutegravir (including as Tivicay). Higher levels of virologic failure were seen in people whose viral load was greater than 100,000 copies/mL when ABC/3TC was used with other anchor drugs, such as efavirenz or boosted atazanavir.

Screening for HLA-B*5701 is necessary before prescribing an abacavir-containing regimen, due to the possibility of abacavir hypersensitivity syndrome. (See Ziagen.)

Coformulated ABC/3TC is available in generic form, which may be less expensive in some situations.

Because of an inconsistent association with the development of cardiovascular disease, Epzicom probably should be avoided by people with known cardiac disease or who are at high risk for its development. (See Ziagen.)

Activist Bridgette Picou: Before starting Epzicom you should have a simple blood test to check for an allergic reaction to the abacavir component of Epzicom. Epzicom is a combination of abacavir and lamivudine, which may be familiar as it is also found in Triumeq. Consideration should be given to your viral load, as Epzicom is most effective if your viral load is less than 100,000 before starting the medication. There are concerns about cardiovascular disease with the abacavir component.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

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

Emtriva

FTC
emtricitabine

✔ Recommended as a component of initial regimen for most people

STANDARD DOSE

One 200 mg capsule once daily without regard to food. According to the label, dosing needs to be adjusted for adults who have decreased kidney function (creatinine clearance less than 50 mL/min). This medication, however, is often used off-label in reduced renal function below 50 mL/min due to the relatively minimal risk of emtricitabine accumulation and side effects. See package insert for guidance on dosing in the setting of kidney impairment. Must be taken in combination with another antiretroviral(s).

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 of 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.

POTENTIAL SIDE EFFECTS AND TOXICITY

Emtriva is very well tolerated. The most common side effects (rarely reported) may include headache, diarrhea, and nausea. Prior to initiation, people should be tested for hepatitis B virus (HBV) infection. Severe exacerbations of hepatitis B have been reported in people co-infected with hepatitis B who have discontinued Emtriva (because emtricitabine also treats HBV). Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted upon Emtriva discontinuation. Call your health care provider right away if you develop any of the following signs or symptoms of hepatitis: 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. 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 medically concerning.

POTENTIAL DRUG INTERACTIONS

Do not take with Cimduo or Temixys, Descovy, Epivir, Epivir-HBV, Hepsera, or Truvada, used for the treatment of hepatitis B. No other significant drug interactions are predicted. Emtriva may be used with hepatitis C drugs such as Epclusa, Harvoni, or Zepatier, depending on the other components in the HIV regimen. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not.

MORE INFORMATION

This drug is used almost exclusively as part of combination tablets. 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, Odefsey, Stribild, and Symtuza). 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, or AZT—very rarely taken today) and Viread or Vemlidy (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.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

200 mg, 30 capsules: $643.82/month
generic: **$579.37**/month

Dr. Melanie Thompson: Emtricitabine, commonly called FTC, is frequently coformulated with other HIV medications in the Gilead stable. In fact, Gilead bought Triangle Pharmaceuticals, the initial developer of FTC, just to acquire FTC for this purpose in 2003. Its resistance pattern is the same as for 3TC, and resistance arises easily without a strong backbone. Initially thought to be slightly more potent than 3TC, this has never been shown to make a clinical difference, and the two drugs are treated as interchangeable for treatment by guidelines panels.

FTC has activity against hepatitis B, and a hepatitis flair could occur if the drug is stopped in people with HBV.

Activist Bridgette Picou: Emtriva is found in many STRs (Biktarvy and Genvoya, for example) and it is similar to lamivudine. It is well tolerated and considered safe, especially where dose adjustment is necessary due to decreased kidney function. Emtriva can also be used to treat hepatitis B, so you should know your hepatitis status or get tested before starting or stopping Emtriva.

GENERIC IS AVAILABLE

Epivir 3TC lamivudine

★ Recommended as a component of initial regimen for most people

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). This medication, however, is often used in reduced renal function below 50 mL/min due to relatively minimal risk of lamivudine accumulation and side effects. See package insert for guidance on dosing in the setting of kidney impairment. Must be taken in combination with another antiretroviral(s).

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 a presumptive 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 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 (10 mg/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 were headache, diarrhea, nausea, malaise (general ill feeling), fatigue, nasal symptoms, and cough. Prior to initiation, people should be tested for hepatitis B virus (HBV) infection. Severe exacerbations of hepatitis B have been reported in people co-infected with hepatitis B who have discontinued Epivir (because lamivudine also treats HBV). Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted upon Epivir discontinuation. Call your health care provider right away if you develop any of the following signs or symptoms of hepatitis: 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.

POTENTIAL DRUG INTERACTIONS

Do not take with Cimduo or Temixys, Descovy, Emtriva, Epivir-HBV, Hepsera, or Truvada, used for the treatment of hepatitis B. No other significant drug interactions. Epivir may be used with hepatitis C drugs Epclusa, Harvoni, 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). Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not.

MORE INFORMATION

This drug is used almost exclusively as part of combination tablets. 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, or AZT—very rarely taken today) and Viread or Vemlidy (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 and Temixys (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), Dovato (with dolutegravir), 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. The availability of generics might also limit choices of therapy. For example, newer brand name drugs and co-formulations, such as Biktarvy, might be restricted to patients who can't physically tolerate generic regimens.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

Epivir 150 mg, 60 tablets:
$498.89/month
generic lamivudine 150 mg, 60 tablets:
$429.66/month
Epivir 300 mg, 30 tablets: **$498.89**/month
generic lamivudine 300 mg, 30 tablets:
$429.66/month

Dr. Melanie Thompson: Lamivudine, commonly called 3TC, is the pharmaceutical long-term survivor of HIV drugs, as the oldest HIV drug still in common use. Its safety profile is excellent and it can be taken once daily. Because it is generic and easily coformulated, it is rarely used in its branded standalone form.

While 3TC is among the best tolerated HIV meds, resistance develops very quickly when not administered with a potent backbone. The M184V mutation arises easily, diminishing the activity of both 3TC and its lookalike FTC, yet it can also make the virus more sensitive to drugs such as TDF and TAF.

3TC has activity against hepatitis B, but resistance emerges more rapidly than for TDF or TAF. A hepatitis flair could occur when stopping the drug in people with HBV. Of note, a separate formulation called Epivir-HBV is for treatment of hepatitis B in people without HIV, and contains only 100 mg of lamivudine. This dose is inadequate for HIV treatment, and should not be interchanged with Epivir.

Activist Bridgette Picou: Epivir can be used with other HIV medications as part of an effective therapy with few side effects and no drug-drug interactions. It can also be used in co-infection with hepatitis B to control it, although it is not a hepatitis B cure. Lamivudine (Epivir) is also found in Triumeq and in Dovato.

GENERIC IS AVAILABLE

Viread

TDF
tenofovir disoproxil fumarate

★ Recommended as a component of initial regimen for most people

STANDARD DOSE

One 300 mg tablet once daily, without regard to food.

For 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, and 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).

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 hepatitis B virus (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 people may experience nausea, diarrhea, vomiting, and gas. Decreases in bone mineral density (BMD) have been observed. BMD monitoring should be considered for 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 bone or kidney problems. Prior to initiation, people should be tested for hepatitis B virus (HBV) infection. Severe exacerbations of hepatitis B have been reported in people co-infected with hepatitis B who have discontinued Viread (because TDF also treats HBV). Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted upon Viread discontinuation. Call your health care provider right away if you develop any of the following signs or symptoms of hepatitis: 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. The Viread formulation contains lactose, which can cause some abdominal discomfort, especially in patients sensitive to lactose. See weight discussion in "More information;" **GO TO** positivelyaware.com/articles/weighty-concerns and positivelyaware.com/articles/fatty-tissues.

POTENTIAL DRUG INTERACTIONS

Do not take with Cimduo or Temixys, Descovy, Hepsera, Truvada, or Vemlidy, all used for the treatment of hepatitis B. Viread decreases 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 Harvoni 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) and TDF with lamivudine (as Cimduo or Temixys) are recommended NRTI combinations by DHHS HIV treatment guidelines for first-time therapy. Tenofovir alafenamide (TAF) has replaced TDF in certain fixed-dose combinations. Biktarvy, Genvoya, Odefsey, and Symtuza are four single-tablet regimens containing TAF instead of TDF. Descovy is similar to Truvada, but it combines emtricitabine with TAF instead of TDF. In clinical trials, TAF had fewer kidney and bone issues than TDF. The NIH reported infants exposed in the womb to TDF may have lower bone mineral content than those exposed to other antivirals. Weight gain is being more commonly recognized as a potential side effect of TAF. In the community, enlargement of the stomach and waist area can be distressing. According to the DHHS HIV treatment guidelines, "Weight gain has been associated with initiation of ART [antiretroviral therapy] and subsequent viral suppression. The increase appears to be greater with INSTIs than with other drug classes. Greater weight increase has also been reported with TAF than with TDF, and greater with DOR than EFV." Other factors have been associated with weight gain in addition to medication used, including race, sex, and previous overweight status. There is no word yet on reversibility, but the race is on to find more answers. 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. Truvada, Cimduo, and Temixys are recommended by DHHS as part of the preferred NRTI combination components of an ART regimen during pregnancy.

Dr. Melanie Thompson: Tenofovir disoproxil fumarate (TDF) revolutionized the nuke "backbones" when introduced in 2001. It was potent, more tolerable in the short term than the old standards AZT, ddI, ddC, and d4T, very durable, and a once daily drug. Its primary companion has been FTC, but now that TDF is off-patent, it is also coformulated with 3TC in drugs such as Cimduo/Temixys, as well as in Delstrigo (along with doravirine.)

TDF can affect kidney function, so laboratory monitoring is necessary. It also causes a slow but predictable decrease in bone density over the course of months, but rarely to a dangerous degree in persons who begin with normal bone density. These side effects appear to be more frequent in the presence of boosters such as ritonavir or cobicistat.

TDF has the interesting side effect of lowering cholesterol levels.

TDF is also potent against hepatitis B and if the drug is stopped, a hepatitis flair can occur.

Activist Bridgette Picou: Tenofovir disoproxil fumarate (TDF), or Viread, is a component of many STRs, and is in Truvada. Monitor your kidneys and bone health while taking Viread, as it is known to affect them over time. Symptoms will often disappear after the medication is stopped.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

300 mg tablets: **$1,504.20**/month
generic 300 mg tablets: **$1,215.94**/month

GENERIC IS AVAILABLE

Ziagen

ABC
abacavir

★ Recommended as a component of initial regimen for most people when used in combination with dolutegravir (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).

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.

➤ 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 simple blood test for HLA-B*5701 should be done prior to starting a regimen containing abacavir to identify people 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 increased risk for HSR, and 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, 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, uncontrolled 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 absolute 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.

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 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

Dr. Melanie Thompson: Had abacavir been developed five years later, it might have been abandoned because of its hypersensitivity syndrome. Intensive scientific effort, however, quickly identified HLA B*5701 as the genetic marker associated with the syndrome, and now a simple screening lab makes it possible to largely avoid this potentially serious side effect. But the need for this one-time screening lab before starting abacavir prohibits its use in rapid ART start regimens.

The hypersensitivity syndrome includes fever, often rash, fatigue, and a variety of other symptoms ranging from respiratory to gastrointestinal. It generally occurs within the first six weeks of starting the drug and can be serious or fatal if the drug is restarted after an initial reaction. People who have had abacavir hypersensitivity should never take it again.

There has been controversy for years about whether abacavir causes or worsens cardiovascular disease, with large studies showing contradictory results. Major guidelines panels including DHHS and IAS-USA agree that the drug should be avoided by people with known cardiovascular disease and those who are at high risk.

Because abacavir is now generic, and generally coformulated with 3TC (Epzicom) or dolutegravir and 3TC (Triumeq), branded Ziagen is rarely used.

It is available as a liquid for people who are unable to swallow pills, or who need dose reduction due to liver disease.

Activist Bridgette Picou: Ziagen, better known as abacavir, it is not intended to be taken alone, but as part of a full regimen. There are potentially harmful, even fatal, reactions associated with abacavir if not checked. There is a blood test for hypersensitivity you should have before use; monitor how you feel once you start Ziagen. If you feel an allergy developing, or just aren't sure you feel right, stop the medication and consult your clinician. You will be tested for lactic acidosis, which is a buildup of acid in the blood.

AVERAGE WHOLESALE PRICE

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

Edurant RPV rilpivirine

✔ Recommended as a 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. For adults and children (12 years of age and older weighing at least 77 pounds, or 35 kg) taking HIV treatment for the first time (treatment-naïve). Must be taken in combination with another antiretroviral(s) which does not contain this medication 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 observed during pregnancy.

According to DHHS guidelines, viral load (HIV RNA) should 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. The CD4 requirement, however, is no longer on the drug label.

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, or a light snack. Taking rilpivirine without food could result in up to 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

Edurant is a very tolerable medication. 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. Stop taking Edurant and see a medical provider right away if allergic reaction or rash occurs with any of the following: fever, trouble breathing or swallowing, blisters, mouth sores, redness or swelling of the eyes, or swelling of the face, lips, mouth, tongue, or throat. 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 both were well tolerated, with Edurant slightly more so. 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, but are very rare. The risk may be greater for people with a history of hepatitis B or C, but may occur 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 dose of the injectable steroid dexamethasone (sometimes given in the ER or hospital). Antacids or other products containing aluminum, calcium carbonate, or magnesium hydroxide 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 such as 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. Edurant should be used with caution when taken with other medications with a known risk for torsades de pointes or QT prolongation (these abnormal heart rhythms can make the heart stop).

MORE INFORMATION

Rilpivirine combined with dolutegravir was approved by the FDA in late 2017; see Juluca. A long-acting injectable formulation of rilpivirine was approved this year along with a long-acting injectable formulation of cabotegravir to form a complete regimen given once a month; see Cabenuva. Edurant is not DHHS recommended for treatment-naïve patients with a pre-treatment viral load greater than 100,000 copies/mL and CD4 T cell count below 200 cells/mm^3. The CD4 requirement, however, is no longer on the drug label. A rilpivirine-based regimen may be advantageous for people with high risk for heart disease due to its relatively low impact on lipid profile. The clinical benefit of these findings has not been demonstrated. While its tolerability and safety profiles are advantages for Edurant, the greater potential for virologic failure in patients with high viral loads, 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 during 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. Melanie Thompson: Rilpivirine largely replaced Sustiva as the leading NNRTI due to its better tolerability, less frequent nervous system side effects (although depression and insomnia are listed as two of its more common side effects), and a different resistance profile.

Today, it is rarely taken as the branded form, but is commonly coformulated as Complera, Odefsey, and Juluca. In addition, the FDA recently approved a long-acting intramuscular injectable formulation of rilpivirine that is taken with cabotegravir for persons with viral suppression and after a 4 week run-in with oral cabotegravir + Edurant (see Cabanuva).

Rilpivirine should not be used as initial therapy if viral load is above 100,000 copies/mL or CD4 less than 200 cells/mm^3 because of higher risk of virologic failure.

Although rilpivirine is generally well tolerated, there are a few important issues to know about in order to maximize success with this drug. For best absorption, it should be taken with a meal. Acid blockers in the proton pump inhibitor category (Prilosec, Nexium, etc.) should not be used. Other acid blockers should only be taken at least several hours before or after the drug. There are a number of important drug interactions with rilpivirine, as mentioned elsewhere on this page, and these should be watched closely, especially when starting and stopping other non-HIV medications.

Kidney stones have been reported with rilpivirine.

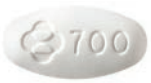
Activist Bridgette Picou: Rilpivirine as Edurant can be found currently in two forms, pill and injectable. In pill form, you will need to take it with food. It is found in Odefsey, Complera, and Juluca. The pill form can be complicated, as non-compliance and missing doses can lead to drug resistance, and cross resistance with another medication. The injectable form is contained in Cabenuva, which is once-monthly dosing.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$1,461.28/month



Pifeltro

DOR
doravirine

✔ Recommended as a component of initial regimen in certain clinical situations (as a component of Delstrigo, or in combination with Descovy, Truvada, Cimduo, or Temixys)

STANDARD DOSE

One 100 mg tablet once daily without regard to food in combination with other antiretroviral drugs in people taking HIV treatment for the first time (treatment-naïve) or to replace the current antiretroviral regimen in those who are virologically suppressed (HIV viral load less than 50 copies/mL) on a stable antiretroviral regimen with no history of treatment failure and no known viral substitutions associated with resistance to doravirine. Must be taken in combination with another antiretroviral(s) which does not contain this medication 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 (with an incidence of 5% or greater) observed in Pifeltro studies were nausea (7%), headache (6%), fatigue (6%), diarrhea (6%), and abdominal pain (5%). Rash, which is a common side effect of the NNRTIs, was reported in up to 2% of the studied population. In the DRIVE-AHEAD study, an in-depth analysis examined 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. Doravirine did not appear to negatively affect cholesterol in studied populations.

POTENTIAL DRUG INTERACTIONS

When taken with the antibiotic drug rifabutin (used for TB and MAC treatment), increase the Pifeltro dose to one 100 mg 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

FDA approved 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 in 2018; 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 tenofovir alafenamide (TAF), found in Descovy, which has potentially less long-term renal and bone toxicity. On the other hand, of course, the use of Pifeltro means the necessity for an extra pill, such as Descovy, or maybe more than one extra pill, depending on the regimen being used. 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 drug class typically has a lower barrier to resistance, as well as extensive cross-resistance. Additionally, the emergence of resistance at the time of virologic failure has been reported with doravirine. Doravirine has tolerability advantages over efavirenz and has relatively favorable lipid effects when compared to both boosted darunavir and efavirenz. It also has fewer potential drug interactions than efavirenz or rilpivirine, and, unlike rilpivirine, virologic efficacy is not compromised among people with high baseline viral loads or low CD4 counts. Doravirine has not yet been directly compared to integrase inhibitor-based regimens in clinical trials. 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. No adequate human data are available yet to establish whether or not Pifeltro poses a risk to pregnancy outcomes. Health care providers are encouraged to register patients to the Antiretroviral Pregnancy Registry (APR) at 800-258-4263.

MANUFACTURER

Merck and Co.
pifeltro.com; (800) 672–6372

AVERAGE WHOLESALE PRICE

$1,825.56/month

Dr. Melanie Thompson: The newest NNRTI, doravirine, was never compared against INSTIs in clinical trials, therefore is not considered a recommended drug for starting treatment by most people. It has some advantages over efavirenz, including fewer nervous system side effects, no food requirements, and no substantial effect on cholesterol.

Pifeltro is now also approved as part of a "switch" regimen for people with suppressed virus and no evidence of prior virologic failure or resistance mutations to drugs in the new regimen.

It is less fussy than rilpiivirine and can be used regardless of viral load and CD4 count, and does not require food or interact with acid blockers. There are some important drug contraindications, though, including with the tuberculosis drug rifabutin, some seizure drugs, the herbal supplement St. John's wort, and enzalutamide (Xtandi), an anti-androgen approved for prostate cancer but also taken by some transgender women.

Recent analyses show no substantial weight gain with doravirine, compared with efavirenz or boosted darunavir.

Pifeltro should not be taken by individuals who are pregnant as there are insufficient data at this time.

Activist Bridgette Picou: Doravirine can be used as both a new start medication or as a stable switch option for fighting HIV. The drug is easy to take and has the benefit of being safe with antacids. It has no restrictions with regard to CD4 or viral load for initiating therapy.

GENERIC IS AVAILABLE

Sustiva EFV efavirenz

✔ Recommended as a component of initial regimen in certain clinical situations (as a component of Atripla, or in combination with Descovy, Truvada, Cimduo, or Temixys)

STANDARD DOSE

One 600 mg tablet once daily, preferably on an empty stomach at bedtime. Must be taken in combination with another antiretroviral(s) that does not contain this medication or medication from the same drug class. Lower 400 mg dose available in the single-tablet regimen Symfi Lo (where it is combined with tenofovir DF and lamivudine; see Symfi Lo page).

Approved for adults and children 3 months and older weighing at least 7.7 pounds (3.5 kg). DHHS guidelines, however, do not recommend use for children aged 3 months up to three years or weighing less than 28.5 pounds (13 kg), due to issues with drug levels; see pediatric guidelines. For children weighing less than 88 pounds (40 kg), the dose is based on weight. See 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 the video at sustiva.com.

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. 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) side effects (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 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 regularly screened for depression and suicidality. Additional side effects may include rash (incidence of up to 26% of adults and 32% of pediatric patients), nausea, vomiting, diarrhea, fever, and gynecomastia (breast development in men). Rash among 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 was not supported by 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

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) (or 520/130 mg twice daily for oral solution) with food when taken with Sustiva. Kaletra cannot be taken once daily with Sustiva. When taken 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 boosted with Norvir. 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. Should not be used with abacavir and lamivudine in patients with baseline HIV viral load over 100,000 copies/mL due to increased risk for virologic failure in this group. 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. May decrease effectiveness of birth control pills; 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 for torsades de pointes. No dose adjustment with Harvoni. Don't take with Epclusa 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. Melanie Thompson: Potent and once daily, Sustiva was once the hottest kid in town, especially when it was combined with TDF and FTC as Atripla. Treating HIV with one pill, once a day revolutionized therapy. The substantial neuropsychiatric effects—vivid dreams, dizziness, depression, suicidality—ultimately were a limiting factor, though.

Ironically, efavirenz was once avoided in pregnancy for concern about birth defects seen in animal studies, but now is among drugs recommended for pregnant persons.

Another niche use for Sustiva is in the treatment of tuberculosis due to lack of drug interactions with TB drugs.

Sustiva increases cholesterol levels.

Efavirenz is now available as a generic combination in Symfi and Symfi Lo.

Activist Bridgette Picou: Sustiva is not a new drug. While potent and with a successful track record, its side effects can be daunting. Feeling tired, headaches, wild dreams, and depression are commonly reported. These may or may not ease over time. But remember that as with all HIV therapy, talk to your clinician if the side effects have an effect on your quality of life. HIV medication should make life more tolerable, not harder.

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.

MANUFACTURER

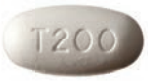
Bristol-Myers Squibb
bms.com; sustiva.com; (800) 321-1335

AVERAGE WHOLESALE PRICE

50 mg, 30 tablets: **$98.12**/month
generic: 50 mg, 30 tablets: **$88.31**/month

200 mg, 90 tablets: **$1,176.74**/month
generic: 200 mg, 90 tablets: **$1,059.07**/month

600 mg, 30 tablets: **$1,176.74**/month
generic: 600 mg, 30 tablets: **$1,073.18**/month



Intelence ETR
etravirine

✔ 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 a meal. 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) that do 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 one 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.

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. 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. The most common side effects in children include rash and diarrhea. Rash is more common in pediatric patients compared to adults, particularly in those less than 6 years of age and females (incidence up to 50% in children 2–6 years old compared to 15% in children 6–18 years old and 10% in adults). Rash is typically described as mild to moderate, pruritic (itchy), with pimple-like skin eruptions. For pediatric patients, rash usually appeared in the second week of therapy and generally resolved within a week. Discuss discontinuing etravirine if fever, blistering, or severe reaction occurs.

POTENTIAL DRUG INTERACTIONS

If Intelence is taken in combination with a protease inhibitor, the PI must be boosted with low-dose Norvir. Intelence 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. Dose 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 rifabutin (Mycobutin) 300 mg daily; however, it should be avoided by people who are also taking a boosted PI. Concentrations of some antiarrhythmics may be decreased when co-administered with Intelence. Intelence and antiarrhythmics should be co-administered with caution. Drug concentration monitoring is recommended, if available. 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. Interaction with Harvoni has not been studied; but based on the metabolism, a clinically significant interaction is not expected. Taking with Zepatier is not recommended. 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

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. 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. DHHS guidelines do not recommend the use of etravirine in treatment-naïve pregnant females. Females who become pregnant while taking etravirine may continue if viral suppression is effective and the regimen is well tolerated. The pharmacokinetics of etravirine are not significantly altered during pregnancy, and no dosage adjustment is necessary. Etravirine is known to have a variable (moderate to high) level of transfer across the human placenta, although insufficient data exists to evaluate the effects on a fetus. Providers are encouraged to enroll pregnant females exposed to antiretroviral medications as early in pregnancy as possible in the Antiretroviral Pregnancy Registry (800-258-4263; apregistry.com).

Dr. Melanie Thompson: Etravirine is not often prescribed these days, but was really helpful to many people when it was released around the same time as darunavir and raltegravir, allowing many people with resistant virus (including with the efavirenz-killing K103N mutation) to have a potent triple-drug regimen that was quite durable. Because etravirine must be taken twice daily (and with food), it is not suitable as initial therapy and was never tested as a first-line drug. It was followed by rilpivirine, which has a number of advantages, including once daily dosing.

Intelence also has complicated drug interactions, so if you are taking it, be sure to check carefully when starting other drugs that may require a change in dosing, either higher or lower.

Activist Bridgette Picou: Etravirine is a second-generation NNRTI basically used for treatment-experienced individuals with resistance to other medications. Its twice-daily dosing and large pill size can be a consideration and barrier for some people. It has a complicated drug interaction list, so keep open communication with your clinician if you add or remove medications (including ones taken over the counter) or have multiple providers.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

100 mg, 120 tablets: **$1,693.80**/month
200 mg, 60 tablets: **$1,693.80**/month

Selzentry

MVC
maraviroc

▼ Recommended as component of ART for treatment of CCR5-tropic virus in treatment-experienced people

STANDARD DOSE

The recommended dose varies depending on other medications being taken but will be either 150, 300, or 600 mg twice daily (available in 150 mg and 300 mg tablets). Can be taken without regard to food. Approved for adults and children weighing at least 4.4 pounds (2 kg) and having a creatinine clearance of at least 30 mL/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. Selzentry for children is dosed based on body weight. See the package insert or DHHS guidelines for weight-based dosing. The oral solution should be administered using the included press-in bottle adapter and oral dosing syringe. Must be taken in combination with another antiretroviral(s).

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. Before starting Selzentry, a specific blood test called a Trofile is required to determine if this medication will work.

➤ 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, pyrexia (fever), upper respiratory tract infections, rash, musculoskeletal symptoms, abdominal pain, and dizziness. Other less common side effects may include allergic reactions, liver toxicity, and heart problems in people with a history of heart disease. Rarely, Selzentry can cause dizziness or fainting when standing up due to low blood pressure. Caution should be used when administering Selzentry in people with a history of or risk factors for postural hypotension, cardiovascular co-morbidities, or taking concomitant medication known to lower blood pressure. 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 level of Selzentry (check with your provider). Selzentry affects immune system cells and could possibly increase the risk of infections and cancer, although this has not been observed in studies with up to five years of follow-up, and some data 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 levels of Selzentry, such as boosted protease inhibitors, Stribild, Genvoya, Tybost, clarithromycin, and itraconazole; 300 mg twice daily if taken with 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 medication Harvoni 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 testing 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 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 people 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. In research bringing Trogarzo to market, Selzentry was often chosen to help create an optimized background regimen. Research participants had extensive HIV drug resistance. 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 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 insurance. ViiV may cover the payment for the Trofile test under certain circumstances. Selzentry seems to have minimal impact on lipid levels. DHHS guidelines do not recommend the use of maraviroc for treatment-naïve pregnant women. Women who become pregnant while taking maraviroc may continue if viral suppression is effective and the regimen is well tolerated.

Dr. Melanie Thompson: The only approved CCR5 receptor blocker is rarely used anymore and is not recommend for first-line therapy. People did well, in general, in the clinical trials that won approval, and Selzentry was well tolerated. Low potency, twice daily dosing, and the need for a tropism test confirming that the virus uses the CCR5 receptor are all barriers to use.

A tropism test is absolutely essential before starting maraviroc, as the drug has no activity against dual/mixed or CXCR4 virus. Unfortunately, many people with more advanced HIV who have been through multiple drug regimens often do not have CCR5 virus. However, it can sometimes be used to cobble together regimens for people with viral resistance. These days, though, fostemsavir will be the first-line "go to" in this setting, yet since it blocks viral entry in different ways, it can be used in combination. (See Rukobia.)

Activist Bridgette Picou: Entry inhibitors block the virus from entering the cell. Maraviroc is not intended for treatment-naïve patients, and has specific conditions for use. A required test (called a Trofile) looks for CCR5 virus type; a different virus type, CXCR4, won't respond to the medication. There may be dose adjustments needed with other medication, including those used to treat HIV. Selzentry is not for everyone, but for those it can work for it is an important option for treatment.

The pharmacokinetics of maraviroc are not significantly altered during pregnancy and no dosage adjustment is necessary. Maraviroc is known to have a moderate level of transfer across the human placenta, although insufficient data exist to evaluate the effects on a fetus. Providers are encouraged to enroll pregnant women exposed to antiretroviral medications as early in pregnancy as possible in the Antiretroviral Pregnancy Registry (800-258-4263; apregistry.com).

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

150 mg, 60 tablets: **$1,867.44**/month
300 mg, 60 tablets: **$1,867.44**/month

Trogarzo

IBA
ibalizumab-uiyk

▼ For heavily treatment-experienced people

STANDARD DOSE

Long-acting antiretroviral 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. An IV push formulation is being studied and would decrease administration time. Trogarzo must be given with an optimized background regimen (OBR). An OBR consists of the best antiretroviral therapy that can be made for a patient based on the patterns of HIV drug resistance of 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%). Select lab abnormalities noted to occur in at least 5% of studied patients were increased bilirubin by greater than 2.6 times ULN (upper limit of normal), 5%; increased creatinine (greater than 1.8 times ULN or 1.5x baseline), 10%; increased lipase (greater than 3 times ULN), 5%; decreased leukocytes, 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 Trogarzo. Renal impairment is not anticipated to affect the pharmacokinetics of Trogarzo.

POTENTIAL DRUG INTERACTIONS

Based on Trogarzo's mechanism of action and pharmacokinetic profile, drug-drug interactions are not expected. No formal drug interaction studies have been conducted with Trogarzo.

MORE INFORMATION

Essentially, this drug is 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. DHHS 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." Trogarzo is a newer option, but it does come with some rules. 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. Patients must be on time. It is expensive because the cost of the drug will be added to other expenses such as the time at the infusion center and cost for qualified individuals to administer and handle the medication, although there may be an option for patients to receive their infusion at home. Infusions can also be done at clinics and at IV centers.

Although given once every two weeks, because it must be used with other HIV medications, antiviral treatment will still be required to be taken daily. Trogarzo 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 there are fewer than 25,000. These are heavily treatment-experienced people who have multi-drug resistance, and have, therefore, limited treatment options. Trogarzo has been shown to work against highly drug-resistant virus, when combined with an OBR. A poster presentation at CROI 2019 showed long-term (96 week) data whereby the safety and efficacy observed at 24 weeks were maintained at Week 96. Fifteen of the 27 participants who continued in the long-term study had achieved undetectable viral load (less than 50 copies) at Week 24, and 16 were undetectable at Week 96. For the study, as part of the OBR, investigational antivirals, including fostemsavir (see Rukobia page), were allowed. Trogarzo also demonstrated CD4 improvements in its clinical studies.

As a biologic, IBA is the first HIV medication made from cells rather than from chemicals. This does not make Trogarzo 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. Trogarzo 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. Trogarzo works against both CCR5 and CXCR4 virus, and may be synergistic with some other classes of antiretrovirals. Resistance test results revealed no evidence of cross-resistance between Trogarzo and any of the approved classes of HIV drugs. Trogarzo is neither metabolized in the liver nor eliminated by the kidneys. Monoclonal antibodies such as ibalizumab are transported across the placenta as pregnancy progresses; therefore, Trogarzo has the potential to be exposed to the developing fetus.

Thera Patient Support can assist with private or government insurance coverage, including AIDS Drug Assistance Program (ADAP), and will also assist in applying any eligible co-pay assistance. Commercially insured patients may be eligible for co-pay assistance and may pay as little as $0. Call (833) 23-THERA (833-238-4372), or GO TO therapatientsupport.com.

Dr. Melanie Thompson: The only approved monoclonal antibody for HIV treatment, ibalizumab blocks the CD4 receptor and prevents the virus from infecting these crucial cells. It is not dependent on CCR5 or CXCR4, and is active against virus resistant to all other HIV drugs. It is only approved for people with highly resistant virus, and at least one other active drug is needed to get durable benefit. The more active drugs, the better.

It is administered intravenously every two weeks, so it is complicated to receive, and is generally administered at infusion centers but can also be arranged through home health in some situations.

A nice feature is that there are no concerns about drug interactions with Trogarzo.

It carries an astronomical price tag of over $100K per year, not counting administration costs, but there is a patient assistance program for drug costs through Theratechnologies.

With better treatments like INSTIs, the number of people with highly resistant virus is relatively small and, hopefully, will continue to decrease if people get the support they need to stay in care and on medication. Therefore, Trogarzo is a little used treatment, but very important for those who need it while waiting for new drug options.

Activist Bridgette Picou: Another newer drug in the HIV fight is Trogarzo. It's fascinating to me the way it fights HIV. It binds to the cell, preventing virus entry by acting like the body's own immune system. The use of this therapy is intended for someone with multi-drug resistance across drug classes. You will continue your current regimen while taking Trogarzo. Getting an infusion every two weeks is a commitment, so you will need to work with your health care team to figure out how best it works for you. Consider your tolerability to needles and infusions before starting.

MANUFACTURER

TaiMed USA

DISTRIBUTED BY

Theratechnologies Inc.
theratech.com; trogarzo.com

AVERAGE WHOLESALE PRICE

$2,969.00 per box (2 vials); 10 vials for loading dose and four vials for continuing dose (every two weeks)

Rukobia

FTR
fostemsavir

▼ For heavily treatment-experienced people

STANDARD DOSE

One 600 mg tablet twice daily without regard to food. For heavily treatment-experienced people with multidrug-resistant virus on a failing HIV regimen due to resistance, intolerance, or safety considerations. Must be taken in combination with another antiretroviral(s).

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. Tablet should be swallowed whole; do not chew, crush, or split tablets.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

At the time of approval, the most common side effect seen was nausea, in 10% of study participants. Other side effects, observed less often, were diarrhea and fatigue. An earlier safety analysis of the Phase 3 BRIGHTE study at Week 96 found that 94% of participants experienced at least one side effect during this Phase 3 study, though most were mild in severity. Moderate to severe side effects had occurred in 21% of participants and included nausea, diarrhea, headache, immune reconstitution inflammatory syndrome (IRIS), vomiting, fatigue, and weakness or lack of energy. Twelve participants had serious side effects that were related to treatment with fostemsavir, and seven percent of participants had side effects that caused them to leave the study. Use with caution in patients who have a history of QTc prolongation (a heart problem). Liver problems can occur, but are very rare. The risk may be greater for people with a history of hepatitis B or C, but may occur in patients without a history of liver disease.

POTENTIAL DRUG INTERACTIONS

Note: new interactions may continue to be discovered after a drug's approval. Dose modification of fostemsavir is not required when co-administering with atazanavir/ritonavir, cobicistat, darunavir/cobicistat, darunavir/ritonavir with and without etravirine, etravirine, maraviroc, raltegravir, ritonavir, or tenofovir DF. Dose modification is also not required when co-administering with buprenorphine/naloxone, famotidine, methadone, norethindrone, or rifabutin (with or without ritonavir). It is not recommended to co-administer with rifampin, an antimycobacterial used for tuberculosis treatment, due to significantly reduced levels of fostemsavir. Cannot be taken with (contraindicated with) enzalutamide (an androgen receptor inhibitor), the anticonvulsants carbamazepine and phenytoin, the cancer drug mitotane, or the herb St. John's wort. Fostemsavir increases concentrations of statins (medications used to treat cholesterol). Use the lowest possible starting dose for statins and monitor for statin-associated adverse effects. Rukobia should be used with caution when taken with other medications with a known risk for torsades de pointes or QT prolongation (these abnormal heart rhythms can make the heart stop). 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. It cannot be taken by trans women on estrogen hormone therapy due to the significantly increased risk for a blood clot. May increase levels of the hepatitis C virus (HCV) drugs grazoprevir and voxilaprevir; however, the magnitude of increase in exposure is currently unknown. Increased levels of grazoprevir may increase the risk of liver enzymes. Use an alternative HCV regimen if possible. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there may be other drug interactions which are not listed here.

MORE INFORMATION

Rukobia is a gp120 attachment inhibitor. A member of the drug class of HIV entry inhibitors, Rukobia works on the gp120 envelope protein that lies on the surface of the virus. It's a necessary part of getting the virus to enter the cell. Rukobia prevents attachment to the CD4 immune cell by blocking gp120 from binding to the CD4 receptor binding sites. This causes the virus to accumulate in extracellular space and is subsequently removed by the body's immune system. Very cool. Watch a video of its mechanism of action at youtu.be/WnreXE-TVi8. Rukobia is designed to be used in highly 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 in July 2018. Dr. Cahn worked on fostemsavir research. Given that Rukobia does not appear to have cross-resistance to any currently approved antiretroviral, as well as its activity regardless of HIV tropism, it is a welcome new drug for patients with very limited treatment options. Rukobia is active against CCR5, CXCR4, and dual-mixed virus (Selzentry is only active against CCR5). In the Phase 3 BRIGHTE study with fostemsavir, study participants all started the trial with treatment failure on the HIV regimen they were taking at the time of entry into the trial. They were heavily treatment experienced with multidrug resistance. Unfortunately, more treatment experience tends to lead to a less likely chance of therapy success later on down the line. This is why medical providers ask patients with HIV to take their meds exactly as prescribed. According to results reported in October 2018, the people in BRIGHTE who were able to add one or two other new drugs to their regimen along with the fostemsavir (called an "optimized background therapy," or OBT), did better than those who only had fostemsavir as a new option. For the OBT group, 54% experienced undetectable viral load at one year of treatment (146 of the 272 OBT participants). For the group just adding fostemsavir, because there was nothing else available that they could add, 38% reached undetectable viral load. This was highly clinically significant for these patients. At the time of approval, 96-week results showed that 60% of the 272 OBT participants had undetectable viral load (less than 40 copies) and an average T cell increase of 205. For the group of 99 participants who only added fostemsavir, 37% had viral load less than 40 at 96 weeks, with an average T cell increase of 119. For individuals with HIV-2, commonly found in some other countries, Rukobia would not be recommended as HIV-2 is inherently resistant to it. For more data, including medications added for optimized therapy, go to the FDA approval announcement at fda.gov/news-events/press-announcements/fda-approves-new-hiv-treatment-patients-limited-treatment-options.

Dr. Melanie Thompson: After many years in development, Rukobia, the first attachment inhibitor, was approved last year for people with multidrug resistant virus and limited options. It is taken twice daily, has few side effects, and does not require food for absorption. It is metabolized in the body into temsavir, the active component.

The BRIGHTE study allowed use of Trogarzo along with fostemsavir and other drugs, so there are some scant data about the combination (along with other drugs), indicating that the combination is safe and can be effective.

Some drugs decrease temsavir levels and can impact Rukobia's activity against HIV, and therefore should not be taken together. These include some seizure medications; enzalutamide (Xtandi), an anti-androgen taken by some transgender women; the tuberculosis drug rifampin; and the herbal supplement St. John's wort.

As is always the case with heavily resistant virus, the more active drugs in the regimen, the more effective and durable Rukobia will be.

Activist Bridgette Picou: Fostemsavir is intended for heavily treatment-experienced people who have multidrug resistance (treatment failure) to multiple medications. Rukobia is a prodrug. This means the drug is metabolized by the body into the active compound. It binds to a protein on the virus itself, gp120, preventing it from entering the cell. The protein is found across multiple virus strains. This may help more patients achieve viral suppression than with regular therapy. It also has a high barrier to drug resistance.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com; rukobia.com
(877) 844-8872

AVERAGE WHOLESALE PRICE

$9,180.00/month

Important Facts About DOVATO

This is only a brief summary of important information about DOVATO and does not replace talking to your healthcare provider about your condition and treatment.

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

If you have both human immunodeficiency virus-1 (HIV-1) and hepatitis B virus (HBV) infection, DOVATO can cause serious side effects, including:

- **Resistant HBV infection.** Your healthcare provider will test you for HBV infection before you start treatment with DOVATO. If you have HIV-1 and hepatitis B, the hepatitis B virus can change (mutate) during your treatment with DOVATO and become harder to treat (resistant). It is not known if DOVATO is safe and effective in people who have HIV-1 and HBV infection.
- **Worsening of HBV infection.** If you have HIV-1 and HBV infection, your HBV may get worse (flare-up) if you stop taking DOVATO. A "flare-up" is when your HBV infection suddenly returns in a worse way than before. Worsening liver disease can be serious and may lead to death.
  - Do not run out of DOVATO. Refill your prescription or talk to your healthcare provider before your DOVATO is all gone.
  - **Do not stop DOVATO without first talking to your healthcare provider.** If you stop taking DOVATO, your healthcare provider will need to check your health often and do blood tests regularly for several months to check your liver.

What is DOVATO?

DOVATO is a prescription medicine that is used without other HIV-1 medicines to treat human immunodeficiency virus-1 (HIV-1) infection in adults: who have not received HIV-1 medicines in the past, or to replace their current HIV-1 medicines when their healthcare provider determines that they meet certain requirements. HIV-1 is the virus that causes Acquired Immune Deficiency Syndrome (AIDS). It is not known if DOVATO is safe and effective in children.

Who should not take DOVATO?

Do not take DOVATO if you:

- have ever had an allergic reaction to a medicine that contains dolutegravir or lamivudine.
- take dofetilide.

What should I tell my healthcare provider before using DOVATO?

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

- have or have had liver problems, including hepatitis B or C infection.
- have kidney problems.
- are pregnant or plan to become pregnant. One of the medicines in DOVATO (dolutegravir) may harm your unborn baby.
  - Your healthcare provider may prescribe a different medicine than DOVATO if you are planning to become pregnant or if pregnancy is confirmed during the first 12 weeks of pregnancy.
  - If you can become pregnant, your healthcare provider will perform a pregnancy test before you start treatment with DOVATO.
  - If you can become pregnant, you should consistently use effective birth control (contraception) during treatment with DOVATO.
  - Tell your healthcare provider right away if you are planning to become pregnant, you become pregnant, or think you may be pregnant during treatment with DOVATO.
- are breastfeeding or plan to breastfeed. **Do not breastfeed if you take DOVATO.**
  - You should not breastfeed if you have HIV-1 because of the risk of passing HIV-1 to your baby.
  - One of the medicines in DOVATO (lamivudine) passes into your breastmilk.
  - Talk with your healthcare provider about the best way to feed your baby.

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

Some medicines interact with DOVATO. Keep a list of your medicines and show it to your healthcare provider and pharmacist when you get a new medicine.

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

What are possible side effects of DOVATO?

DOVATO can cause serious side effects, including:

- **Those in the "What is the most important information I should know about DOVATO?" section.**
- **Allergic reactions. Call your healthcare provider right away if you develop a rash with DOVATO. Stop taking DOVATO and get medical help right away if you develop a rash with any of the following signs or symptoms:** fever; generally ill feeling; tiredness; muscle or joint aches; blisters or sores in mouth; blisters or peeling of the skin; redness or swelling of the eyes; swelling of the mouth, face, lips, or tongue; problems breathing.
- **Liver problems.** People with a history of hepatitis B or C virus may have an increased risk of developing new or worsening changes in certain liver tests during treatment with DOVATO. Liver problems, including liver failure, have also happened in people without a history of liver disease or other risk factors. Your healthcare provider may do blood tests to check your liver.
  Tell your healthcare provider right away if you get any of the following signs or symptoms of liver problems: your skin or the white part of your eyes turns yellow (jaundice); dark or "tea-colored" urine; light-colored stools (bowel movements); nausea or vomiting; loss of appetite; and/or pain, aching, or tenderness on the right side of your stomach area.
- **Too much lactic acid in your blood (lactic acidosis).** Lactic acidosis is a serious medical emergency that can lead to death. **Tell your healthcare provider right away if you get any of the following symptoms that could be signs of lactic acidosis:** feel very weak or tired; unusual (not normal) muscle pain; trouble breathing; stomach pain with nausea and vomiting; feel cold, especially in your arms and legs; feel dizzy or lightheaded; and/or a fast or irregular heartbeat.
- **Lactic acidosis can also lead to severe liver problems,** which can lead to death. Your liver may become large (hepatomegaly) and you may develop fat in your liver (steatosis). **Tell your healthcare provider right away if you get any of the signs or symptoms of liver problems which are listed above under "Liver problems." You may be more likely to get lactic acidosis or severe liver problems if you are female or very overweight (obese).**
- **Changes in your immune system (Immune Reconstitution Syndrome)** can happen when you start taking HIV-1 medicines. Your immune system may get stronger and begin to fight infections that have been hidden in your body for a long time. Tell your healthcare provider right away if you start having new symptoms after you start taking DOVATO.
- **The most common side effects of DOVATO include:** headache; nausea; diarrhea; trouble sleeping; tiredness; and anxiety.

These are not all the possible side effects of DOVATO. Call your doctor for medical advice about side effects.

SO MUCH GOES INTO WHO I AM

HIV MEDICINE IS ONE PART OF IT.

Why could DOVATO be right for you? DOVATO is proven to help control HIV with just 2 medicines in 1 pill. That means fewer medicines* in your body while taking DOVATO. It's proven as effective as an HIV treatment with 3 or 4 medicines.
Learn more about fewer medicines at DOVATO.com

DOVATO is a complete prescription regimen to treat HIV-1 in adults who have not received HIV-1 medicines in the past or to replace their current HIV-1 medicines when their doctor determines they meet certain requirements.

Results may vary.

*As compared with 3- or 4-drug regimens.

Dovato
dolutegravir 50 mg/
lamivudine 300 mg tablets

Morgan

Taking DOVATO

Compensated by ViiV Healthcare

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

Where can I find more information?

- Talk to your healthcare provider or pharmacist.
- Go to DOVATO.com or call 1-877-844-8872, where you can also get FDA-approved labeling.

August 2020 DVT:4PIL

New to treatment? Considering a switch?

Ask your doctor about DOVATO.

Descovy for PrEP

FTC/TAF
emtricitabine/tenofovir alafenamide

★ FDA approved for the prevention of HIV

STANDARD DOSE

For HIV-negative adults and adolescents weighing at least 77 pounds (35 kg) for the prevention of HIV. At this time, Descovy for PrEP is not FDA approved for the prevention of HIV for individuals assigned female at birth. Take one tablet once daily, without regard to food. The tablet contains 200 mg emtricitabine and 25 mg tenofovir alafenamide.

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 for PrEP is not recommended if CrCl is between 15 to less than 30 mL/min or under 15 mL/min if you are not on dialysis.

➤ SEE EMTRIVA, which is contained in Descovy.
➤ SEE PACKAGE INSERT for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

The most common adverse event is diarrhea, observed in up to 5% of individuals given Descovy in the large DISCOVER study that led the FDA to approve Descovy for PrEP. There was also nausea (4%) and headache, fatigue, and abdominal pain (2% each). Check for hepatitis B virus (HBV) before taking Descovy and vaccinate against it if appropriate. If Descovy is discontinued abruptly in people with hepatitis B virus, flare-up of hepatitis may occur—talk to your provider before discontinuing. Drug resistance to HIV therapy may develop if people going on Descovy for PrEP unknowingly already have HIV, or if infection occurs after starting PrEP. However, drug resistance was rare in the extremely few individuals who acquired HIV during the DISCOVER trial (seven out of 2,670 persons on Descovy and 15 out of 2,665 on Truvada). All were in the Truvada arm and all were in those with baseline HIV infections. As with previous PrEP studies, DISCOVER found the effectiveness of Descovy for PrEP was related to drug adherence—taking Descovy daily for PrEP as prescribed. The TAF component in Descovy is associated with relatively decreased risk for toxicity to the kidneys and bones (such as decreases in estimated glomerular filtration rate, or eGFR, and bone mineral density, or BMD) when compared to TDF in Truvada. Kidney function (including creatinine clearance, or CrCl) should be monitored while taking Descovy for PrEP. Recommended monitoring also includes STI screening. When comparing TDF versus TAF, bone changes may be of greater concern for young people whose bone structure is still growing and for older individuals who may be becoming frail. Kidney changes may be of greater concern for individuals who have pre-existing kidney problems or older individuals at risk of developing kidney problems. Stigma remains a significant concern of HIV prevention, especially PrEP. When taken for HIV treatment, tenofovir has been associated with weight gain; see Descovy page.

POTENTIAL DRUG INTERACTIONS

Do not take with any other HIV or HBV drugs (including Vemlidy, or TAF) when using Descovy for PrEP. Avoid taking Descovy with drugs that negatively affect the kidneys, including chronic use or high doses of anti-inflammatory drugs for pain such as Advil or Motrin (ibuprofen) and Aleve (naproxen). Descovy for PrEP can be used with the hepatitis C drugs Harvoni or Zepatier. Monitor for tenofovir toxicities if used with Epclusa. Descovy should not be taken with certain anticonvulsants (including carbamazepine, oxcarbazepine, phenobarbital, and phenytoin), rifabutin, rifampin, rifapentine, or St. John's wort. Concentrations of tenofovir, FTC, and other substances that clear the body through the kidneys could be increased (along with risk of toxicity) by the aminoglycoside antibiotics and the antivirals acyclovir, cidofovir, ganciclovir, valacyclovir, and valganciclovir. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not.

MORE INFORMATION

In December, DHHS perinatal guidelines added a new section on PrEP for periconception, antepartum, and postpartum periods. Descovy for PrEP was not approved for the prevention of HIV via receptive vaginal sex. This is because the effectiveness of Descovy for PrEP was not evaluated in this context. Studies with cisgender women and adolescent girls are underway. The tenofovir alafenamide (TAF) in Descovy and the tenofovir disoproxil fumarate (TDF) in Truvada (the first PrEP medication on the market) absorb, distribute, and concentrate differently in the body, but both are highly effective against the virus whether for treatment or prevention. In the meantime, Truvada, which is now available as a generic, is FDA approved for PrEP against HIV for all populations, including for use in receptive vaginal sex. Descovy for PrEP was only studied in men who have sex with men (MSM) and transgender women (5,387 MSM and 74 transwomen) in the DISCOVER study that brought Descovy for PrEP to market. TAF has less of a negative effect on renal function and bone mineral density than TDF, but the long-term clinical significance of the changes observed with the two medications remains unknown. Medical providers, however, prefer TAF over TDF for certain patients who may be at higher risk for renal and bone toxicity (including youths and older individuals). There are considerations for using PrEP even with U=U (Undetectable equals Untransmittable). A guide to help providers bill for PrEP services is available at nastad.org/resource/billing-coding-guide-hiv-prevention. Two excellent websites for finding a PrEP provider are preplocator.org and aidsvu.org—although any provider can prescribe PrEP. For more information, GO TO cdc.gov/hiv/basics/prep.html. 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 $7,200 a year; contact the patient assistance hotline at (877) 505-6986, or GO TO gileadadvancingaccess.com. PrEP Facts: Rethinking HIV Prevention and Sex is a closed Facebook group for people interested in or currently on PrEP, and their allies.

Dr. Melanie Thompson: A head-to-head comparison of Descovy to Truvada in gay and bisexual men and transgender women showed that Descovy was not inferior to (or not worse than) Truvada for preventing HIV. The study did not include cisgender women, transgender men, or people who inject drugs, and they are not included in the FDA approval for Descovy. A study is underway internationally to address efficacy and safety in cis-gender women.

Slightly lower rates of kidney side effects and decline in bone density were seen with Descovy, similar to results from HIV treatment studies. Also, as with treatment, HDL and LDL cholesterol and weight were slightly higher with Descovy than with Truvada. Weight gain was about 1 kg (2.2 lbs.) higher than with Truvada at 48 weeks. The long-term clinical impact of these findings is not clear.

Initially, there was some misunderstanding about the study results, and some "spin" that Descovy was better than Truvada in preventing HIV. This is not true. And, especially for younger people without diseases that predispose them to kidney problems (diabetes, hypertension, for example), Truvada is safe and may be a preferable choice. TDF/FTC now is available off-patent and could impact cost.

Some people prefer the smaller pill size of Descovy.

Descovy has not been studied as intermittent treatment and is only approved when taken once daily.

Activist Bridgette Picou: Descovy serves dual roles as an HIV medication and an HIV prevention med. As pre-exposure prophylaxis, it prevents the transmission of HIV. Descovy is a smaller pill and requires less medication (TAF vs. TDF) than its predecessor, Truvada. This means less toxicity, sparing bone density and kidney health. This drug is not indicated as a prevention method for persons at risk for HIV who have vaginal intercourse. More study is needed for that. Descovy also does not prevent other sexually transmitted infections (STIs), so plan on regular monitoring of kidney health and STI testing while using Descovy. Do not skip doses as this increases chances of seroconversion.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$2,316.85/month

GENERIC IS AVAILABLE

Truvada for PrEP

FTC/TDF
emtricitabine/tenofovir DF

★ FDA approved for the 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 CrCl 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 observed 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 usually reversible upon stopping Truvada. In adolescents, however, BMD-z scores (which compare bone growth to that of matched peers) did not return to baseline. 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 bone or kidney 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. When taken for HIV treatment, tenofovir may be associated with weight gain; see Truvada page.

POTENTIAL DRUG INTERACTIONS

Do not take with any other HIV or HBV drugs (including Vemlidy, or TAF) when using Truvada 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

In December, DHHS perinatal guidelines added a new section on PrEP for periconception, antepartum, and postpartum periods. A new PrEP drug was approved in October 2019—see Descovy for PrEP page. Truvada for PrEP is almost 100% effective in preventing HIV when taken daily as recommended. Stigma and lack of access to health care continue to fuel HIV infections. Remember, risk depends on the situation—including where you live. Other problems include not knowing about PrEP and inability to perceive a need for it (not realizing one may have vulnerabilities at all). Although the drug label specifies prevention of 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). The label notes that risk includes a number of behavioral, biological, or epidemiological factors, including condomless sex, current or past STIs, self-identified risk, having sexual partners of unknown HIV status or unknown HIV viremic status, or sexual activity in a high prevalence area or network. Screening and monitoring requirements include checking for STIs and hepatitis B and C. 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—although any provider can prescribe PrEP. 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 $7,200 a year; contact the patient assistance hotline at (877) 505-6986, or GO TO gileadadvancingaccess.com. Truvada generic became available in the U.S. in October 2020. See discussion online of the generic's pricing. PrEP Facts: Rethinking HIV Prevention and Sex is a closed Facebook group for people interested in or currently on PrEP, and their allies. For more information, GO TO cdc.gov/hiv/basics/prep.html.

Dr. Melanie Thompson: Approved in 2012 for HIV prevention, Truvada is up to 99% effective at preventing new HIV infections when taken daily with high adherence. Studies also indicate that intermittent treatment (2 doses within 12 hours prior to sex, and one dose on each of the following 2 days) can be effective, although this strategy has not been studied in, and is not recommended for, cis-gender women.

Truvada is currently the only approved drug for PrEP in cis-gender women.

The same side effects seen in treatment have been seen in the prevention setting, with a small decline in bone density and a small decline in kidney function. From the DISCOVER trial, we learned that lipids and weight are also slightly lower than for Descovy.

It should be noted that generic TDF/3TC (Cimduo/Temixys) can be substituted for treatment but has not yet been studied as PrEP. However, generic TDF/FTC from Teva can be substituted for Truvada. The cost is only slightly lower than branded Truvada, but Teva provides a co-pay card to help with out-of-pocket costs.

Activist Bridgette Picou: Truvada as PrEP is taken once daily. Adherence is important with PrEP. Missed doses decrease effectiveness, thereby increasing the chance of seroconverting. The TDF (disoproxil fumarate) requires monitoring for kidney toxicity and bone density. These effects build up over time, so the longer you are on therapy, the more important it is. Testing for STIs will also be done at three-month intervals, when it's time for your 90-day refill. Truvada can be used for all groups of people at risk of acquiring HIV whether engaging in vaginal or anal sex.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$2,210.74/month
generic: **$2,100.20**/month

non-HIV | **Indicated for the reduction of excess abdominal fat** in adults living with HIV who have lipodystrophy

Egrifta SV

tesamorelin for injection

STANDARD DOSE

1.4 mg, injected subcutaneously (under the skin) daily in stomach (abdominal) area, rotating the site for each injection and avoiding scar tissue, bruises, and the navel. A step-by-step administration guide and video are available at egriftasv.com.

A potential complication of HIV, antiretroviral therapy, or growth hormone (GH) deficiency may cause a fat redistribution of adipose tissue known as lipohypertrophy (a form of lipodystrophy). Abdominal lipohypertrophy is defined by an accumulation of excess visceral abdominal tissue (also called "hard belly") surrounding all abdominal organs (liver, stomach, pancreas, etc.). Hard belly is a different type of fat compared to subcutaneous fat (regular, or soft, fat). Excess visceral abdominal fat may be linked with serious health issues like cardiovascular disease, cognitive decline, diabetes, dyslipidemia, non-alcoholic steatohepatitis (fatty liver disease), or increased mortality risk, and may make it hard to perform certain daily activities.

Hard belly may be a complicated term to accurately describe and can be mistaken for general weight gain or obesity. To understand if you are at risk, talk with your health care provider, who can assess the risk in two easy steps. Step one: feel your belly to see if it is hard. Step two: measure your waist and hip circumference to calculate a waist-to-hip ratio.

Unlike growth hormone (GH) products, Egrifta SV is an analogue of human growth hormone-releasing hormone (GHRH), which stimulates the pituitary gland to produce and secrete the body's own GH. Egrifta SV reduces visceral abdominal fat while preserving subcutaneous fat. The effect appears after three months, increases at six months and is sustained for 12 months.

The effect on visceral abdominal tissue was seen in two Phase 3 clinical trials. A post-hoc responder analysis has shown, on average, a reduction in waist circumference of 1.85 inches and 31% of decrease in visceral abdominal fat. It is important to note that visceral abdominal fat returns in a few months once tesamorelin is discontinued.

Egrifta SV should not be administered to patients who have a pituitary gland tumor, surgery, or other pituitary gland problems; active cancer; hypersensitivity to either tesamorelin or ingredients in tesamorelin; who are pregnant or become pregnant; or are less than 18 years old. Egrifta SV should be used with caution in patients who have a history of cancer or problems with blood sugar or diabetes, and should be discontinued in critically ill patients.

The most common side effects include pain in legs and arms, and muscle pain. Despite initial concerns that tesamorelin may have significant drug-drug interactions with medications that use CYP450 (a liver enzyme) for metabolism, a study in healthy volunteers proved otherwise. Patients need to be monitored for potential interaction. Long-term safety of the heart and the blood vessels is unknown. Each dose necessitates mixing 2 mg vials stored at room temperature with 0.5 mL of sterile water for injection. Do not use Egrifta SV if the solution is discolored, cloudy, or contains visible particles. Once reconstituted, the vial should be rolled gently, not shaken, between the hands for 30 seconds to ensure mixture is a clear, colorless solution, and is administered right away. If not used immediately, the reconstituted Egrifta SV should be discarded.

CAP & PAP INFORMATION

Co-pay covers up to $7,000 a year. If someone is having difficulty paying for Egrifta SV, there are several programs available through Thera's patient support at (833) 23-THERA (833-238-4372), Monday–Friday, 8:30 a.m.–8 p.m., EST or at therapatientsupport.com or egriftasv.com.

MANUFACTURERS

Theratechnologies, Inc.
egriftasv.com

Thera Patient Support:
(833) 23-THERA; (833-238-4372)
therapatientsupport.com

AVERAGE WHOLESALE PRICE

$6,932.40/month

non-HIV | **Anti-diarrheal** approved for use in those with HIV/AIDS and on antiretroviral therapy

Mytesi

crofemeler

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 three 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 INFORMATION

Co-pay program:
(877) 336-4397
Pay no more than $25, maximum benefit of $6,000 per year.
PAP: (888) 527-6276;
mytesi.com

MANUFACTURER

Napo Pharmaceuticals
mytesi.com; (844) 722-8256

AVERAGE WHOLESALE PRICE

$2,647.34/60 tablets

Serostim

somatropin for injection

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 take 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 (which would require 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 vision changes, headache, nausea, or vomiting). Serostim should be avoided by people 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 malignancy changes.

Rotate injection sites to avoid injection site reactions. An injection training program is available; GO TO serostim.com/treatment-with-serostim or call 877-714-2947. 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 and metabolized, there are some potential drug-drug interactions, though no formal drug studies have been conducted. These theoretically potential interactions can affect people 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 such as 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 INFORMATION

There are several assistance programs, including the 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, refreshed this year with more healthy living resources, injection tips, and advice for talking with your provider. See also hivwasting.com.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

6 mg: 7 injections (usually a one-week supply)
$5,142.82

The road ahead

What's on the horizon—new drugs in development

Recently approved

Vocabria (cabotegravir)
Oral formulation of an integrase inhibitor mainly used for lead-in dose before long-acting formulation and possibly for bridging when injectable Cabenuva cannot be taken. It will not be available for other purposes. From ViiV/Janssen.

Cabenuva (cabotegravir LA/rilpivirine LA)
Two long-acting drugs from INSTI and NNRTI families that are given by intramuscular injection and that have very long half-lives—detectable after more than one year following single dose. CAB LA + RPV LA injections were studied for treatment, and CAB LA is being studied for prevention as single INSTI injection. From ViiV/Janssen. See drug page in this guide.

Rukobia (fostemsavir)
gp120 attachment inhibitor, twice daily oral antiretroviral taken in combination with other antiretrovirals. For multi-drug resistant HIV. From ViiV. See drug page this guide.

Phase 3

islatravir/3TC/doravirine
Fixed-dose combination of the NNRTI doravirine plus generic 3TC and new NRTI islatravir (EFdA). Current studies used triple combination for initial ART and switch to islatravir/doravirine for dual maintenance ART. From Merck.

islatravir/doravirine
Dual FDC with NNRTI doravirine. Current studies look at switch option after viral suppression with triple-drug ART. From Merck.

leronlimab (PRO 140)
Monoclonal antibody CCR5 target. Once-weekly (350–700 mg) subcutaneous injection being studied in addition to oral ART for multi-drug resistance and as monotherapy maintenance therapy (without oral ART). From CytoDyn.

Phase 2/3

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

lenacapavir (GS-6207)
New drug class (capsid inhibitor) with activity at multiple stages of viral lifecycle. Subcutaneous injection every six months. It is being studied simultaneously for treatment and prevention. From Gilead.

Phase 2

GSK3640254
A maturation inhibitor with Phase 2a results in HIV-positive participants. From ViiV.

Phase 1–3 and pre-clinical

3BNC117, 10-1074, PGDM1400, PGT121, 10E8, UB-421, etc.
Many bNAbs (broadly neutralizing antibodies) are in development for HIV prevention, treatment, and cure, often in dual or triple combination (see "Scenes from the bNAb Revolution" in the January+February 2020 issue). Potential as switch option without ART and in current studies for use as PrEP.

Albuvirtide + 3BNC117
Albuvirtide is a fusion inhibitor, approved in China, that is being developed in the U.S. by Frontier Biotechnologies in combination with the bNAb 3BNC117 for use in treatment-experienced patients.

Phase 1 and pre-clinical

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-1156
Once-daily unboosted protease inhibitor; high potency, long half-life, potential for fixed-dose combination single-tablet regimen. From Gilead.

MK-8583, MK-8504
Tenofovir prodrugs, both with completed Phase 1 studies. From Merck.

ADAPTED FROM
HIV Pipeline 2020: New Drugs in Development, published by HIV i-Base, March 2020. For the full report, GO TO i-base.info/htb/3722

ABBREVIATIONS

3TC: lamivudine
ART: antiretroviral therapy
bNAb: broadly neutralizing antibody
FDC: fixed-dose combination
INSTI: integrase inhibitor
mAb: monoclonal antibody
NNRTI: non-nucleoside reverse transcriptase inhibitor
NRTI: nucleoside reverse transcriptase inhibitor
PI: protease inhibitor

HABEEB MUKASA

Is it HARD BELLY?*

HARD BELLY isn't regular fat. If you are living with HIV, learn the difference – find a specialist and make sure you're heard.

*Also known as excess visceral abdominal fat

THERA technologies

727-01-03/20 – 7,875x10,75

my HARD BELLY

ROADSIDE ASSISTANCE

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 known 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 tables on the following pages are adapted from NASTAD's "HIV Pharmaceutical Company HIV Patient Assistance Programs and Cost-Sharing Assistance Programs": nastad.org/resource/hiv-cap-and-pap.

GULNARA USSENOVA/ISTOCK

COST-SHARING ASSISTANCE PROGRAMS (CAP)

DRUGS COVERED	MANUFACTURER AND CONTACT INFORMATION	ASSISTANCE	RENEWAL
Kaletra and **Norvir**	**AbbVie** 800-441-4987, option 5; kaletra.com; norvir.com	**Kaletra:** Co-payment assistance covers up to the first $400 per prescription per month. **Norvir:** Covers up to $1,200 a year for co-payments.	
Temixys	**Celltrion** temixys.com		
Atripla, **Biktarvy**, **Complera**, **Descovy**, **Emtriva**, **Genvoya**, **Odefsey**, **Stribild**, **Truvada**, **Tybost**, and **Viread**	**Gilead Sciences** 877-505-6986; gileadadvancingaccess.com	**Biktarvy, Descovy, Genvoya, and Truvada:** Covers the first $7,200 per year of co-payments. **Atripla, Complera, Odefsey,** and **Stribild:** Covers the first $6,000 per year of co-payments. **Emtriva** and **Viread:** 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.	Rolls over on January 1
Edurant, **Intelence**, **Prezcobix**, **Prezista**, and **Symtuza**	**Janssen Therapeutics** 866-836-0114; janssencarepath.com; edurant.com; intelence.com; prezista.com; prezcobix.com; symtuza.com	Covers the first $7,500 per year (for Symtuza, it's $12,500) of co-payments, deductibles, and co-insurance.	Automatic renewal
Delstrigo, **Isentress**, **Isentress HD**, and **Pifeltro**	**Merck and Co.** 800-444-2080; isentress.com	Covers the first $6,800 of co-payments, deductibles, and co-insurance for each of 12 eligible prescriptions.	Enrollment is valid until coupon expires, 12/31/2021
Cimduo, **Symfi**, and **Symfi Lo**	**Viatris** 877-446-3679 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; trogarzo.com; therapatientsupport.com	Contact program for details	
Cabenuva, **Dovato**, **Juluca**, **Lexiva**, **Rescriptor**, **Retrovir**, **Rukobia**, **Selzentry**, **Tivicay**, **Tivicay PD**, **Triumeq**, **Trizivir**, **Viracept**, and **Ziagen**	**ViiV Healthcare** 844-588-3288; ViiVConnect.com	**Cabenuva**, $13,000; **Dovato** and **Juluca**, $6,250; **Tivicay**, $5,000; and **Triumeq** and **Rukobia**, $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 $3,400 per year. Patients may apply for a second grant during their eligibility period subject to availability of funding. All HIV funds are closed. Can only get on a wait list.	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; boehringer-ingelheim.us	500% FPL
Temixys	Celltrion temixys.com	
Atripla, Biktarvy, Complera, Descovy, Emtriva, Genvoya, Odefsey, Stribild, Truvada, and **Tybost**	**Gilead Sciences*** 800-226-2056 gileadadvancingaccess.com	500% FPL
Edurant, Intelence, Prezcobix, Prezista, 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; isentress.com	400% FPL
Trogarzo	**Theratechnologies** 833-238-4372; trogarzo.com	Call program for details
Cabenuva, Combivir, Dovato, Epivir, Epzicom, Lexiva, Juluca, Rescriptor, Retrovir, Rukobia, 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.

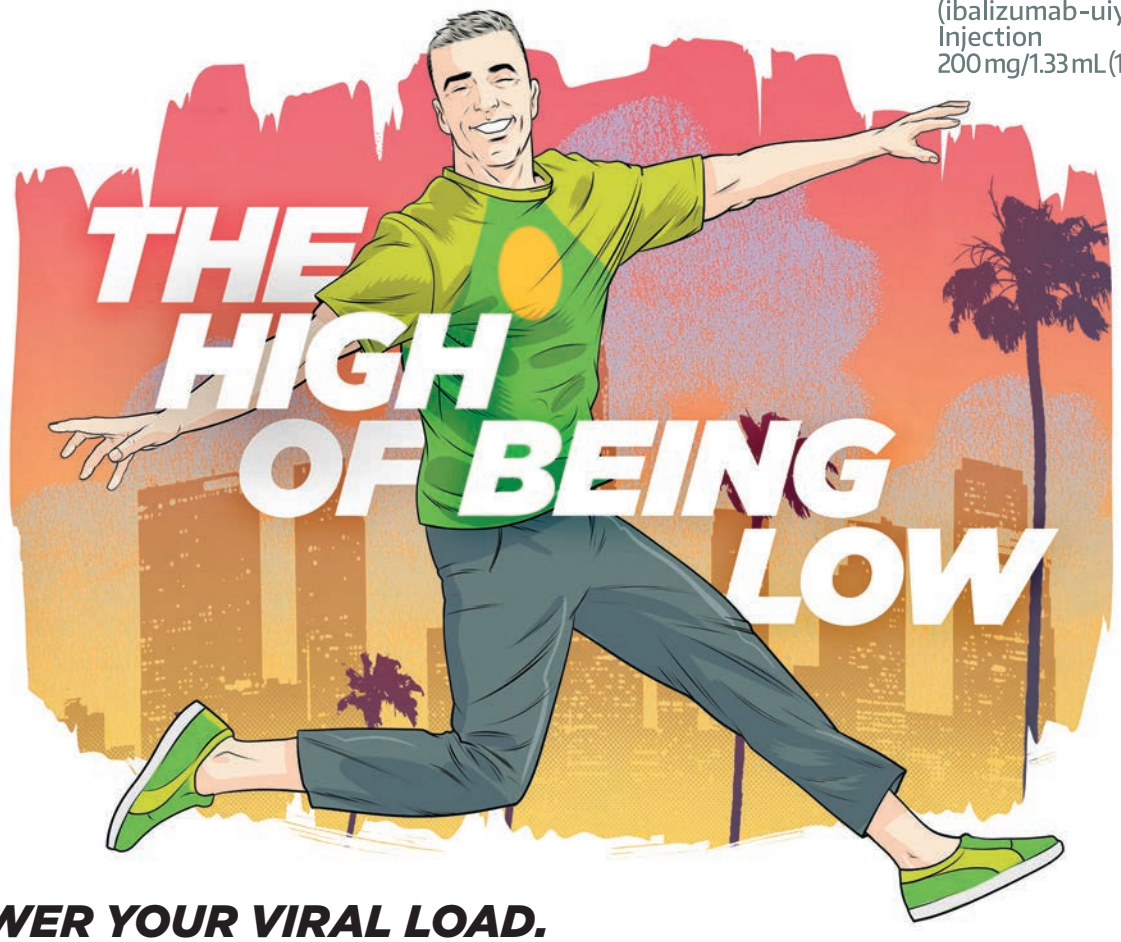
Fair Pricing Coalition (FPC)
fairpricingcoalition.org
Negotiates with companies to ensure that cost-sharing and patient assistance programs are adequately generous and easy to apply for.

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.

NASTAD
nastad.org
Leading non-partisan non-profit association that represents public health officials who administer HIV and hepatitis programs in the U.S.

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.

Trogarzo®
(ibalizumab-uiyk)
Injection
200 mg/1.33 mL (150 mg/mL)



LOWER YOUR VIRAL LOAD. AND MAKE UNDETECTABLE A POSSIBILITY AGAIN.*

* Undetectable viral load is defined as fewer than 50 copies of HIV per mL of blood.

Ask your healthcare provider about TROGARZO® –
A fully active HIV-1 treatment designed specifically for those with treatment failures

For more information, visit TROGARZO.com

WHAT IS TROGARZO®?
TROGARZO® (ibalizumab-uiyk) is a prescription medicine that is used with other antiretroviral medicines to treat Human Immunodeficiency Virus-1 (HIV-1) infection in adults who:

- have received anti-HIV-1 regimens in the past, and
- have HIV-1 virus that is resistant to antiretroviral medicines, and
- who are failing their current antiretroviral therapy

It is not known if TROGARZO® is safe and effective in children.

IMPORTANT SAFETY INFORMATION
Do not receive TROGARZO® if you have had an allergic reaction to TROGARZO® or any of the ingredients in TROGARZO®.

TROGARZO® can cause serious side effects, including:

- Allergic reactions. TROGARZO® can cause allergic reactions, including serious reactions, during and after infusion. Tell your healthcare provider or nurse, or get medical help right away if you get any of the following symptoms of an allergic reaction: trouble breathing, swelling in your throat, wheezing, chest pain, chest tightness, cough, hot flush, nausea or vomiting.
- Changes in your immune system (Immune Reconstitution Inflammatory Syndrome) can happen when you start taking HIV-1 medicines. Your immune system might get stronger and begin to fight infections that have been hidden in your body for a long time. Tell your health care provider right away if you start having new symptoms after receiving TROGARZO®.

The most common side effects of TROGARZO® include diarrhea, dizziness, nausea, and rash. These are not all the possible side effects of TROGARZO®.

Before you receive TROGARZO® (ibalizumab-uiyk), tell your healthcare provider about all of your medical conditions, including if you are:

- **Pregnant or plan to become pregnant.** It is not known if TROGARZO® may harm your unborn baby. Tell your healthcare provider if you become pregnant during treatment with TROGARZO®.
- **Breastfeeding or plan to breastfeed.** You should not breastfeed if you have HIV-1 because of the risk of passing HIV-1 to your baby. Do not breastfeed if you are receiving TROGARZO® as it is not known if TROGARZO® passes into breast milk. Talk with your healthcare provider about the best way to feed your baby during treatment with TROGARZO®.

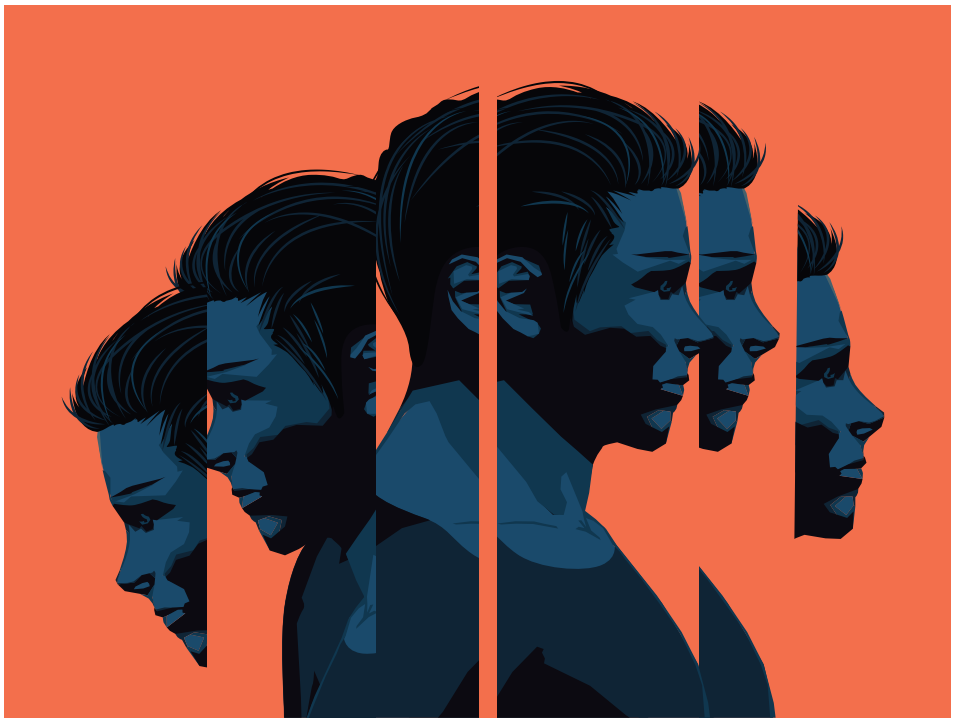
Also tell your healthcare provider about all the medicines you take, including all prescription and over-the-counter medicines, vitamins, and herbal supplements.

For more information or medical advice about side effects, ask your healthcare provider. You may report side effects to the FDA at 1-800-FDA-1088 or the THERA patient support® program at 1-833-238-4372.

THERA technologies

POZ ADVOCATE
SCOTT SCHOETTES
@PozAdvocate

Getting back to (discrimination free) work



With the ever-widening availability of COVID vaccination, the U.S. has slowly started to emerge from the worst of this pandemic. A decreasing number of daily deaths and progression toward "herd immunity" should signal a return to work for many who were without a job as a result of the pandemic. Welcome news undoubtedly—and a good time to talk about HIV discrimination in the workplace.

For many years, people living with HIV have called Lambda Legal's Help Desk more about employment discrimination than any other subject. With that in mind, here are some helpful things to know about HIV and the workplace.

First—and most important—employment discrimination based on HIV status is illegal under federal law. The Americans with Disabilities Act (ADA)—alongside another statute called the Rehabilitation Act, which applies to employers who receive federal funding—protects everyone in the U.S. from HIV discrimination in employment, regardless of the state in which the person works. There may also be state laws that protect against employment discrimination based on HIV status, but they are in addition to the protections provided under federal law.

Even though the ADA has the word "disabilities" in its name, its protections apply to all people living with HIV. It doesn't matter whether a person is considered disabled for purposes of social security or state disability benefits. The definition of "disability" under such benefits statutes is different from the definition used under the ADA. Under the ADA, everyone living with HIV falls within the protections of the law, regardless of their viral load, T cell count or other measure of immune health or physical abilities.

There is not a job in the world that a person living with HIV cannot safely perform.

Second, there is not a job in the world that a person living with HIV cannot safely perform. The primary routes of HIV transmission—sexual contact, sharing injection drug paraphernalia, and perinatal activities (e.g., giving birth, breastfeeding)—are not things that most people do as part of their job. And for those who do engage in an activity at their job that may present some level of transmission risk, such as a sex worker or a doctor performing surgery, those risks can be nearly eliminated by the proper use of universal precautions. The ADA prohibits employment discrimination unless doing the job presents a *significant* risk to the health or safety of others—and HIV never presents that degree of risk in the workplace.

Third, a person living with HIV (or any other covered disability under the ADA) can ask for a reasonable accommodation if their HIV is interfering with their ability to do the job. In general, to secure the protections of the ADA, a person has to be able to perform the essential duties of the job despite their disability. But there is an important caveat to that requirement: if providing the person with a *reasonable* accommodation—such as a schedule modification due to medication side effects or time off for medical appointments—would allow the person to perform the essential functions of the job, the employer must provide that accommodation.

What is considered "reasonable" is determined on a case-by-case basis and will generally need to be supported by a letter from a doctor explaining why the accommodation is required under the circumstances. The medical professional need not identify the

precise condition at issue in the initial letter—just that there is a medical condition requiring the accommodation. If the employer pushes back, the employee may have to decide whether they want to reveal the precise nature of the disability creating the need for an accommodation—in this case, HIV—but there is no need to reveal this information out of the gate.

Fourth, an employer cannot ask an applicant questions that may reveal a disability—or send an applicant for a physical or medical exam—until the employer has made an offer of employment *conditioned solely on the answers to those questions or the result of the exam*. The purpose of this rule under the ADA is to make it very clear when the employer's decision not to hire is based on the answers to those questions or the results of the medical exam. That way, after learning about the person's HIV status (or other disability), the employer can't claim that they didn't hire the person for some other reason, such as failure to pass a background check.

What do you do if they ask questions that will reveal your HIV status or send you for a medical exam before making you a conditional offer of employment? That is a great question, to which there is no easy answer. If an applicant points out that such an inquiry or exam is illegal under the ADA or refuses to answer or participate in the exam, there is a pretty good chance the person won't get a job offer at all. And suing to enforce this specific provision of the ADA is not particularly realistic. On the other hand, answering the questions or participating in the exam may lead to the very type of discrimination that the ADA prohibits. That would require a lawsuit as well, but such a lawsuit has a better chance of succeeding.

Whatever you do, don't lie. Refusing to answer a question or to complete parts of the pre-exam medical form is fine, but lying about your HIV status could make it more difficult to succeed in court. Even if you think your HIV status is irrelevant to your ability to perform the job—and, as discussed above, in most instances it will be—you are better off answering truthfully or not at all. If the employer can show that you lied about this one thing, they can paint you as a liar with respect to other things you are claiming in your lawsuit.

Even if you think your HIV status is irrelevant to your ability to perform the job—and...in most instances it will be—you are better off answering truthfully or not at all.

In this day and age, most employers are not going to ask such inappropriate questions, so you shouldn't have to worry unless you are applying for a very few particular jobs. Your HIV status is pretty much irrelevant to your ability to do any job—even the job of military service member (more on that in a future column)—so happy job-hunting!

SCOTT SCHOETTES lives openly with HIV and is the HIV Project Director at Lambda Legal, where he engages in impact litigation, public policy work, and education to protect, enhance, and advance the rights of everyone living with HIV.

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Travel companions

Associate editor **Enid Vázquez** recalls memorable moments from 25 years of the HIV drug guide

I'll never forget watching a co-worker take a new-and-improved HIV medication many years ago. The moment the pills hit his mouth, his face scrunched up with a look that said, "Yuck!"

"What's wrong?" I asked him.

"It starts melting in my mouth and it tastes nasty," he said.

I was so disappointed. This was supposed to be a kinder, friendlier new protease inhibitor that he was taking, Viracept. But there was no mention in any press release or in the package insert about yuckiness.

Which is why we try to take up the slack in information with the POSITIVELY AWARE HIV drug guide (and in other issues throughout the year as well). What are people living with HIV really experiencing when they take their meds?

Sure, HIV medications are needed. And we know they ain't candy. But to have to go through what he went through, well, that's hard.

I've worked on each of the 25 drug guides. I like to think of it as helping people prepare for what to expect. Sometimes, to help strengthen their resolve to stick with therapy. Always to provide useful information.

The first time Viracept appeared in the drug guide, in 1998, activist Spencer Cox of the Treatment Action Group wrote, "Nelfinavir comes in blue tablets that begin to dissolve as soon as they touch moisture. This can be annoying if your hands happen to be damp, and downright nauseating if you don't manage to swallow them on time."

I wrote in the drug guide two years later, "Tablets begin to dissolve immediately in your mouth—yucky."

I'm sure the word "yucky" doesn't pass muster with the FDA.

As for the diarrhea side effect, official information didn't quite cover the explosiveness of some of the PIs. How about this from that Viracept page in 2000: "Do not leave the pharmacy without anti-diarrhea medication available without a prescription, such as Imodium. Take a change of clothes with you when you leave home for the first several weeks." Yikes.

It may be too informal for the FDA, but it worked for our pharmacist reviewer, who helped me hammer out that statement.

"Tastes like motor oil" we wrote about the liquid formulation of Norvir. That's what people told me, and pharmacists confirmed it. Although, I always wondered how anybody knew. Sure, Norvir liquid has a look and a smell and a texture, but how the hell does anyone know what motor oil tastes like? Still, we got it. And we warned you.

'Tastes like motor oil' we wrote about the liquid formulation of Norvir.

It's not always bad news.

Take Complera with food, we tell you. But one person's doctor in Chicago prescribed it to be taken on an empty stomach. When he brought it up with his pharmacist, the pharmacist agreed with the doctor. Drug guide in hand, he had his social worker iron out the problem.

One woman told me that her doctor was not helpful when she experienced rash with Agenerase. Then she read our drug guide and saw that Agenerase has a sulfa component. She has a sulfa allergy. Mystery solved.

These stories are scary, but they're another reason why we produce the drug guide—and every issue of POSITIVELY AWARE. To give people a fighting chance in their health care. People could look at the drug label, but a community-based magazine is easier to follow. To be fair, the health care system needs the help. Providers are overwhelmed.

For all the effort I put into the drug pages, and the hard work of the pharmacists who review it and write it, I know that people love looking at the doctor and activist comments first.

Some activist reviewers are dry, but some are descriptive, making for some memorable moments.

"It's good to know that there are options like this should I ever need it, but it also reminds me to take my little three-pill once-a-day regimen faithfully," wrote Cathy Olufs in 2007, on Fuzeon, a medication that had to be injected twice daily.

"The first time I took Sustiva I was attending a meeting and the room was literally spinning. The drug's biggest misfortune is its 'altered state' side effect and the fact that it will do you no good if you've been on the other NNRTIs," wrote Matt Sharp in 2002.

My all-time favorite witty line came from Heidi Nass, and is apropos for the car theme of this issue.

In the 2005 drug guide, she wrote, "If 3TC were a car and turned up on 'Pimp My Ride,'* it would be unveiled by Xzibit at the end of the show as FTC—newly tricked out, for sure, but the same under the hood."

Funny or (usually) not, it's been 25 years of tweaking HIV treatment with new information and changing paradigms. Or, as I like to think of POSITIVELY AWARE in general, saving lives—and saving health. It's been a fascinating journey on a road that continues to wind in new and interesting ways. See you here at some of the road stops.

* "Pimp My Ride" was a popular television show that ran on MTV from 2004–2007.

ISTOCK

Four tips for older adults aging with HIV

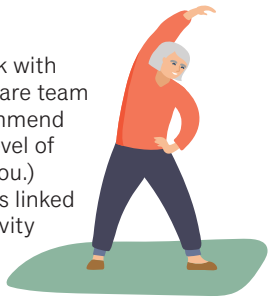
BY JOSHUA J. MATACOTTA, PSYD, CAHIMS

Thanks to recent advances in medicine and science, getting older with HIV can be a lot like ... getting older without HIV. Most adults aged 65 years and older are living with more than one chronic health condition, such as diabetes, heart disease, hypertension, arthritis, depression, or cancer. Learning about a new medical condition or complication with treatment can be overwhelming. Here are four healthy aging tips for people with HIV:

1. Seek out information and ask questions. Keep up to date with the latest information about living with HIV by following reputable sources for news, updates, and information. Go to your medical appointments with questions or things that are bothering you.

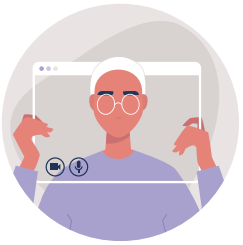
2. Use technology to stay informed about health status. Most healthcare systems or medical practices offer an online patient portal that lets a person email their healthcare team, schedule and track appointments, request medication refills, and view lab results. Keep an eye on your latest CD cell counts (CD3, CD4, CD8), HIV RNA levels (viral load), complete blood count (CBC), platelet counts, markers of liver and kidney function, and other relevant information. Keep in mind that trends are often more important than a single lab result. If you have any concerns, ask your care team about the results and how treatment of one medical condition can affect another condition.

3. Get—and stay—active. The American College of Sports Medicine recommends that adults aged 65+ engage in 30 minutes of moderate-intensity physical activity most or all days of the week. (Check with your healthcare team if they recommend a different level of activity for you.) Research has linked physical activity with healthy aging and reduced risk of chronic disease. Regular exercise can boost your mood, energy level, and self-confidence. And a bonus!—physically active older adults are less susceptible to viral and bacterial infections, suggesting that exercise improves immune system function.



Feeling lonely or isolated is no fun—and isn't good for your health either.

4. Connect with others. Feeling lonely or isolated is no fun—and isn't good for your health either. Social support and connection with others are associated with better physical and mental health. Stay connected with family and friends by meeting up in person, talking on the phone, or chatting online. It may also help to connect with others living with HIV to share your experiences.



Whether you are currently venturing into aging with HIV territory or see it on your horizon, remember it is completely manageable. Living and aging well with HIV does require some help. Use your curiosity to find the latest information about HIV and aging, and always ask questions. Technology and other resources can help you manage appointments and stay informed about your health status. And remember to stay active—physically and socially—to stay well and feel well.

This article originally appeared on the Society of Behavioral Medicine website, sbm.org. Reprinted with permission.

DR. JOSHUA J. MATACOTTA trained as a clinical psychologist with an emphasis in behavioral medicine and health psychology. He has trained and worked in community mental health, university student health centers, hospitals, and public schools. Currently, he is an assistant professor at Western University of Health Sciences in the College of Health Sciences, and is the Data Analytics Section Chief in the Department of Population Health at the College of Osteopathic Medicine of the Pacific. He teaches part-time in the psychology department of Pasadena City College. Professional service includes President of the Board of Directors at IBHRI, and serving as a scientific reviewer for the NIH Division of AIDS, Behavioral, and Population Sciences study section.

ISTOCK

If you are living with HIV, ask yourself the following questions:

Have I lost weight?

- [ ] Have I lost weight without trying?
- [ ] Does the change in my weight impact how I feel about myself or my health?
- [ ] Is my clothing looser than before because I have lost weight without trying?
- [ ] Have those I know mentioned that my appearance has changed?

Do I have less energy?

- [ ] Are any of my usual activities more difficult to perform?
- [ ] Am I exercising less than in the past?
- [ ] Do I need to take a break more often?
- [ ] Do I tire more easily after certain activities?

If you answered "yes" to any of these questions, take this questionnaire to your next appointment with your healthcare provider to start a conversation about HIV-associated wasting and to inquire about treatment. Together you can discuss next steps. To learn more about HIV-associated wasting, visit: **IsItWasting.com**

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