Separated and isolated by a pandemic, we still reach out for community
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.

Michael Broder is a 60-year-old gay male who tested positive for HIV in 1990. He grew up in Coney Island (think: *Requiem for a Dream*). As an undergrad, he attended Columbia University on a Pulitzer Scholarship. He earned an MFA in poetry from NYU in 2005, and a PhD in Classics from CUNY in 2010. His dissertation was on queer kinship and camp aesthetics in Roman satire. He loved three men who died of AIDS—Randy Snyder, universally beloved ACT UP activist; Tony Salinas, who played bass with the rock band Mountain; and Marcos Betancourt, who was on track to ignite the world. He married the poet Jason Schneiderman in 2004, in Provincetown, Massachusetts, one of the first few hundred gay men to get legally civilly married in the United States. Currently getting same-sex divorced, he lives in historic Bed-Stuy, Brooklyn, with a number of feral cats, and the best roommate ever. His book of poems, *This Life Now*, was a finalist for the Lambda Literary Award for gay poetry in 2015.

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.
Editor's Note

Jeff Berry
@PAeditor

I'm grateful to have lived to see the day where this revolution in treatment is now upon us, because this is only the beginning.

Gratitude

This is the 26th Annual Positively Aware HIV Drug Guide. I'm incredibly honored to have served as editor on 18 of these incredible resources for people living with HIV and those who care for them. This HIV Drug Guide has some changes to it that we think you'll like. For the first time we've added HIV PrEP to the HIV Drug Chart that's in the middle of this issue (we added the PrEP drug pages to the guide itself a few years ago). We've included a statement on Paxlovid from our amazing physician for this year's guide, Dr. Melanie Thompson. Paxlovid is the latest oral medication (under emergency use authorization and not yet approved) to treat mild to moderate COVID for those at highest risk for severe disease. It contains an old HIV drug (Norvir) that has a lot of interactions with other drugs, so see the statement on page 17 for more information.

Treatment and prevention for HIV continues to evolve with long-acting injectable medications now or soon to be on the market. As this issue went to press, Cabenuva, the first long-acting injectable regimen for treatment of HIV, was approved for dosing every other month—that's six doses a year! Wow! What a long way we've come from handfuls of pills two or three times a day with dreadful side effects—some of which weren't all that effective. I'm grateful to have lived to see the day where this revolution in treatment is now upon us, because this is only the beginning. Monoclonal antibodies, gene-editing technology, mRNA vaccines for HIV, implants, etc.—all of these advances are mind-blowing and moving at a rapid pace, and will result in this guide having to evolve as well. A pill chart may soon become a relic of the past in the not-too-distant future. We'll have to come up with a lot of new categories, symbols, icons—but it's all good, and it will be exciting to be a part of the future of the HIV treatment and prevention landscape.

This is where I have to stop and point out once again (I know, I sound like a broken record) that none of it will lead us to the end of the HIV epidemic unless people have access to these new therapies. We have to ensure health equity for our Black and Brown brothers and sisters and for all communities that are disproportionately affected by HIV. Pricing of these drugs cannot continue to grow exponentially by leaps and bounds as the advances in research have—it is just not sustainable, not for our health systems, and not for our pocketbooks. Will these new modes of delivery and novel therapies only be accessible for the privileged few, while the rest of us are left to swallow generic versions of old HIV pills because that’s all our plans will cover or that we can afford? Let's hope not.

I'm also honored to work with a great team that puts this behemoth together year after year, Enid Vázquez and Rick Guasco. You know I love you guys! We drive each other crazy as we get down to the wire to meet our deadline, but it's all worth it because of the end result. We do it for all for you, the people who are reading this right now!

Enid wanted to make sure that we gave a special shout out and thank you to all of the scientists and providers who make her sister's continued life and well-being possible. That goes for all of us living with HIV—we all thank you for making our lives your life's work. We wouldn't be here (literally) if it wasn't for you.

Wherever life leads us, let's continue to express gratitude to each other and for what each of us brings to the table. I'm grateful for my postal carrier who delivers the mail (almost) every day. I'm grateful for my therapist who encourages me to keep working on getting in touch with my best self (and letting go of the rest). I'm grateful for my coworkers who make me laugh and teach me new things every day (at least when I'm in the office). I'm grateful for family and friends who help me feel connected and keep me grounded. And above all I'm grateful to the universe for providing—always.

Thanks to you, our readers, for subscribing to the magazine, for reading my ramblings, and for joining along with us for this wild ride. Last but not least, we're grateful to the frontline workers who are doing the work each and every day on behalf of people living with and affected by HIV. Our community has never been stronger, and I'm so grateful to have been welcomed into it with open and loving arms.

Always take care of yourself, and each other.

Jeff Berry
The problem is how you see the problem

I have a question: Is your HIV a problem for you? Why or why not? If I asked you to identify the biggest problem it causes for you—could you? Is it stigma? Internalized stigma? Medication adherence? Is it navigating relationships (including the one with yourself)?

Next questions: How long have you been living with HIV and the same problem(s)? Have your coping skills evolved? Has your “problem” changed face over the years, or is it the same one or two on repeat?

Which leads me to this: What skills do you use to cope with HIV as a concept, lifestyle, and life process? Don’t worry, I’m not about to tell you what to do or how to do something about it; I’m not a therapist, and I damn sure don’t have all the answers. I am, however, working on me and how I see myself, and I just wanna make you take stock of your life with HIV for a second and do the same.

Consider this notion—which is actually one of my personal affirmations: The problem is how you see the problem. The Google definition of problem is “a matter or situation regarded as unwelcome or harmful and needing to be dealt with and overcome.”

Just reading the words “harmful” and “overcome” invokes some angst, right? I came across a definition once that seems less negative as it processes through the brain’s gray matter: A problem is the difference between what is and what could or should be.

How about that for seeing a problem differently? I don’t know about you, but “what could or should be” makes me feel a little optimistic as opposed to putting me in the struggle mindset of having to overcome. Problem solving involves looking at the problem, defining and analyzing the underlying concerns, then using your skills to facilitate change.

All too often in HIV we let the virus—and other people—define us. They label us and come to conclusions about a life they’ve never lived—and we let them. We get caught in endless cycles of what we know life could or should be, and yet let stigma and shame corner us into feeling differently. For example, sometimes I would resent taking a pill every day because I didn’t want to depend on a thing for my health. I’ve reframed the problem—it’s now my opportunity each day to ensure I’m here to do what my purpose says I need to do and I’m more grateful and gracious about it.

Another good example is love. I hear women say pretty often “he loves me even with HIV” or “he loves me in spite of HIV.” In my head I’ve also reframed that idea of being loved in spite of HIV and changed it to being loved with HIV. When we do things “in spite of,” it implies a certain disdain for the thing in question. It’s that you don’t like it, but you’ll tolerate or live with it anyway. The problem with allowing that is it’s an insidious and subtle kind of stigma, both external and internalized. You’ll settle for less than you deserve in a relationship because after all, you do have this thing that needs to be worked around. I don’t want to be tolerated on any level, and in a relationship, we better be working through, not around, issues that arise. Love the whole imperfect package or leave me alone. The problem isn’t HIV makes love and relationships hard. The problem is my relationship with those things and HIV.

So, let me ask again: Is your HIV a problem, or is how you see the problem your problem?

Be well. You matter.
THE 26TH ANNUAL HIV DRUG GUIDE
MARCH+APRIL 2022

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‘As a Black trans woman who has been living with HIV for over 10 years, I just want to say it’s okay to be nervous and overwhelmed, but dig deep and find that determination and tenacity to survive and thrive so you, too, can motivate and inspire others.’

—MALLERY JENNA ROBINSON (SECOND FROM RIGHT, WITH CARLOS MORENO, ANDREA DE LANGE, DAMONE THOMAS, AND OLIVER WONG, PAGE 3

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.
SHARE OR RECYCLE
THIS MAGAZINE.

positivelyaware.com/subscribe | MARCH+APRIL 2022 5
From the AIDS epidemic of the 1980s through today’s COVID pandemic, people living with HIV have endured isolation in one form or another while reaching for community to find support, information, and hope. We might be alone, but we’re also together.

That was the theme behind the Los Angeles photo shoot for the cover (and additional photos) of the 26th annual HIV Drug Guide, which brought together people living with HIV—both recently diagnosed and long-term survivors—and care providers in the HIV field, all passionate about their work, and some living with HIV as well. They each make a unique contribution, finding a place in the communities they serve.

“I have been an HIV advocate since first volunteering in the food pantry of an HIV service organization, nearly eight years ago,” says Danielle M. Campbell, MPH, an activist and faculty member of the Charles R. Drew University of Medicine and Science, a historically Black college, as well as at UCLA and the University of California at San Diego.

“Learning how HIV disproportionately impacted women of African descent globally, the decision to pursue this work was a logical conclusion. So many of my people were being affected, I couldn’t resist joining the ranks alongside others doing this work,” she adds.

At 34, Damone Thomas’ HIV journey has taken him from Kingston, Jamaica, where he tested HIV positive in January 2008, to L.A, where he is now a health care worker and a retention specialist.

“My turning point in facing life with HIV came in September 2011,” he says. “I decided I wanted to live, because there is so much to gain. Today, I thrive above HIV.”

As an undergrad at California State University, Northridge, Alfredo “Freddy” Favela, MPH, was passionate about sexual health, often advocating on campus for safer-sex practices. Pursuing his master’s degree in public health with an emphasis in epidemiology at Los Angeles Pacific University, he began focusing on communities of color. Favela is now community outreach supervisor and community
engagement lead at UCLA’s CARE Center.

In 2011, Mallory (“Mally”) Robinson was studying for a double bachelor’s degree in biology and history in Montgomery, Alabama, when she collapsed at the restaurant where she worked. Two weeks later, she learned she was living with HIV. “I was completely overwhelmed as a then-21-year-old Black trans woman, but I was determined to not let this diagnosis deter me from living my best life,” she says. Today, she advocates for women of all trans identities and is a member of the Los Angeles County Commission on HIV.

“As a Black trans woman who has been living with HIV for over 10 years, I just want to say it’s okay to be nervous and overwhelmed,” she says, “but dig deep and find that determination and tenacity to survive and thrive so you, too, can motivate and inspire others.”

Being public about his status helped Oliver Wong, 30, overcome isolation and stigma. Diagnosed barely a year ago, he’s even made it part of his schtick. “As a stand-up comedian, I also talk about being HIV positive,” he says. “It helps me to share my experience onstage. It’s very therapeutic, empowering, and freeing to talk about. If you’re living with HIV and turn your experience into art and share it with the world, it’s gonna not only help you, but also help the world understand HIV and remove stigma.

“If you are newly diagnosed, it’s important to talk with someone who has been living with HIV for a longer time,” he says. “Hearing firsthand experiences from a long-term survivor can give you assurance that HIV is manageable.”

Carlos Moreno, 31, came out to his family, friends and coworkers by telling his story onstage during a concert by the Reveille Men’s Chorus in Tucson, Arizona, in May 2015. “My entire life changed after that,” says Moreno, whose pronouns include he and they. “I no longer carried the heavy burden of secrecy. This opened up many doors for me, and just a couple months after coming out, I moved to Los Angeles to continue expanding my advocacy.”

For him, being visible means representing. “Folks needed to see people like myself living well, working, and thriving with HIV, as well as contributing to the field of service delivery for marginalized populations. This was something that I struggled to see in the early years of my diagnosis.

“Not everyone gets the chance or has the privilege to be out about their status, or to be a community advocate,” they acknowledge, “but know the rest of us do what we do because we love and honor you, and carry you with us.”

It was 1987, and Andrea de Lange didn’t fit “the type” who would have HIV. She had swollen lymph nodes, and her new doctor was trying to rule out possible causes. A cancer screening three years earlier had turned out negative.

“My doctor never thought I could be HIV positive when I got the biopsy, because I didn’t fit the stereotypes of who was HIV positive, and he also didn’t know about my past history with the boyfriend,” she says.

“The boyfriend,” an injection drug user, had turned her on to crystal meth, telling her that she needed to lose weight. The relationship lasted from 1981 to 1985, but she was already in another abusive relationship. “Starting a year before I was diagnosed, he treated me like a leper after I told him my status,” she says. “I let him live with me and treat me that way for another two years because I was so unempowered and thought I’d never be in a better relationship.”

Today, de Lange has been happily married for more than 19 years, “to an HIV-negative guy, who totally loves and accepts me, HIV and all,” she says.

After decades of practicing safer sex, Nicholas Snow says it was one moment that led to him acquiring HIV in August 2007. “I remind myself that I am human, and this was a human experience,” he says. “I don’t beat myself up for it, and I am loving and forgiving of myself. My greatest power is my ability to live and express my truth.

“My personal mission statement is to honor and express my creativity in a way that makes a difference,” says Snow, producer and host of PromoHomo.TV, an LGBTQ online platform.

“My status doesn’t weigh on me personally, except that stigma and ignorance are still pervasive within the gay male community, which makes it challenging to find love, but I haven’t given up,” he adds. “What about U=U [undetectable equals untransmittable], the message that a person with undetectable viral load is not able to transmit HIV to a sexual partner] don’t they understand?”

In medical school, Alicia Morehead-Gee, MD, MS, 34, was fascinated by the global impact of HIV/AIDS. At UCLA, her work focuses on HIV prevention and Black women. Today, she’s medical director of HIV prevention for AltaMed Health Services to expand PrEP (pre-exposure prophylaxis) awareness and access. “My team trains primary care providers, pharmacists, and staff on PrEP and PEP (post-exposure prophylaxis),” she says.

A young single mother of two, struggling to work and go to school, Dawn P. McClendon shifted gears from becoming a lawyer to promoting public health and to become part of something larger than herself. Now 48, she is assistant director of the Los Angeles County Commission on HIV.

“I am eternally changed by the relationships I have built with people living with and impacted by HIV as well as those who are a part of this workforce, and I am forever grateful,” she says.

José Magaña’s love of helping people helped him to overcome stigma. He learned of his HIV status about six years ago while getting tested to get onto PrEP.

“I told my sexual partner, and they did not want anything to do with me,” he says. “It took me a year of therapy to learn to love myself regardless of my status, whether people choose to accept me or not. Since then, I decided to educate and share my story with others to get rid of HIV stigma.”

At 39, public service has always been part of José Magaña’s life. He’s been in the Army National Guard for 17 years, having spent over a year and half on deployment assisting hospital workers during the COVID-19 pandemic. He’s now a community organizer for The Wall Las Memorias Project, focusing on substance abuse and mental health, and facilitates a virtual group for people living with HIV that meets every Wednesday night via Zoom.

“I love to help people in the community that I am part of,” he says. “Everyone has a different story to tell and it’s important to share those stories so that others can learn and grow from them.”

ABOUT THE PHOTOGRAPHER

Mark Harvey is a visual artist, designer, photographer, and educator living in Los Angeles. He also teaches a variety of topics in graphic design and photography at the Art Center, Pasadena City College, Glendale College, and at Los Angeles City College.
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 that the amount of 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 the virus can do to your immune system so you’ll stay healthier longer. It also means you can’t transmit HIV to your partner through sex when you are on antiretroviral treatment (ART) and undetectable at less than 200 copies for at least six months (undetectable equals 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 starting 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, if you’re undetectable, 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 naive”), but they are not for everybody, including some people who are treatment-experienced or have multi-drug resistance. A fixed-dose combination (FDC) combines two or more ARVs in one pill but is not always an entire regimen (an STR is a type of fixed-dose combination). We now have a long-acting injectable regimen (Cabenuva), which at press time consists of a one-month oral lead-in followed by two intramuscular injections administered every four weeks. Other long-acting drugs are in development; for one that’s expected to be approved this year, see lenacapavir, page 32.

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 at your local HIV organization or support network. That includes housing and job opportunities if you need them. Anti-stigma efforts are also important for HIV care.

7. **What is drug resistance?**

If treatment is not taken correctly or is unable to completely suppress the virus, it 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, are easier to take, and have few if
any side effects. However, it is better to avoid missing doses. Drug resistance may lead to the need for more complicated therapy (such as more pills).

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; you and your health care provider will have to decide which drugs to use.

Here are a few tips that can help you talk with your doctor to 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, treatment 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) on each drug page 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.”) The drug cost-sharing and patient assistance program charts (beginning on page 62) include information on how to access programs that can help cover all or part of the costs of many 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; PEP must be started within 72 hours after a recent possible exposure. “PrEP” stands for “pre-exposure prophylaxis” and is taken daily to prevent someone from getting HIV. “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, either prescription or over-the-counter, GO TO hiv-druginteractions.org. Among the good community-based sources 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.

1. **BINDING**
   - HIV binds to the surface of a host cell.
   - **ENTRY INHIBITORS**

2. **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
     - PRO-140 (CCR5 receptor)
     - albuvirtide

3. **REVERSE TRANSCRIPTION**
   - Viral DNA is formed by reverse transcription.
   - **NRTIs** and **NRTTIs (nukes)**, including these in development:
     - islatravir
     - elusufavirine

4. **INTEGRATION**
   - Viral DNA is transported into the host cell’s nucleus and integrates into the host’s DNA.
   - **INTEGRASE INHIBITORS**
     - GS-9883

5. **REPLICATION**
   - New viral RNA is used as genomic RNA and to make viral proteins.

6. **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

7. **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:
     - lenacapavir
   - **MATURATION INHIBITOR** in development:
     - GSK3640254

*IN MARCH 2021, RESEARCHERS ACCEPTED THAT THE CAPSID UNCOATS IN THE NUCLEUS
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, or Tivicay plus 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.

**Recommended initial regimens in certain clinical situations**

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

**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
- 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
- Prezempix: DRV/c
- Stribild: ETV/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
Recommended initial regimens in certain clinical situations (continued)

Boosted PI + 2 NRTIs
(In general, boosted DRV is preferred over boosted ATV.)

- **Syntuza**
  - DRV/COBI/FTC/TAF B1

- **Prezobix**
  - DRV/COBI

- **Prezista**
  - DRV 800 mg

- **Norvir**
  - RTV

- **Descovy**
  - FTC/TAF

- **Truvada**
  - FTC/TDF

- **Evotaz**
  - ATV/COBI

- **Reyataz**
  - ATV

- **Norvir**
  - RTV B1

- **Descovy**
  - FTC/TAF

- **Truvada**
  - FTC/TDF

- **Prezobix**
  - DRV/COBI

- **Prezista**
  - DRV 800 mg

- **Norvir**
  - RTV B2

- **Epzicom**
  - ABC/3TC

  - if HLA-B*5701 negative

- **NNRTI + 2 NRTIs**

- **Delstrigo**
  - DOR/3TC/TDF B1

- **Pifeltro**
  - DOR B3

- **Descovy**
  - FTC/TAF
### Recommended initial regimens in certain clinical situations (continued)

#### NNRTI + 2 NRTIs

3TC may substitute for FTC and vice versa

<table>
<thead>
<tr>
<th>Regimen</th>
<th>NRTI + NNRTI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atripla</td>
<td>EFV 600 mg / FTC / TDF B1</td>
</tr>
<tr>
<td>Symfi</td>
<td>EFV 600 mg / FTC / TDF B1</td>
</tr>
<tr>
<td>Symfi Lo</td>
<td>EFV 400 mg / FTC / TDF B1</td>
</tr>
<tr>
<td>Sustiva</td>
<td>EFV 600 mg B2</td>
</tr>
<tr>
<td>Descovy</td>
<td>FTC / TAF B2</td>
</tr>
</tbody>
</table>

**If viral load is less than 100,000 copies/mL and CD4 count is more than 200 cells/mm³**

**Odefsey**

<table>
<thead>
<tr>
<th>Regimen</th>
<th>INSTI + NRTI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symfi Lo</td>
<td>EFV 400 mg / FTC / TDF B1</td>
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<tr>
<td>Odefsey</td>
<td>RPV / FTC / TAF B2</td>
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**Complera**

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<thead>
<tr>
<th>Regimen</th>
<th>INSTI + NRTI</th>
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<tbody>
<tr>
<td>Symfi Lo</td>
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</tr>
<tr>
<td>Complera</td>
<td>RPV / FTC / TAF B1</td>
</tr>
</tbody>
</table>

### 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.

<table>
<thead>
<tr>
<th>Regimen</th>
<th>INSTI + NRTI</th>
</tr>
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<tbody>
<tr>
<td>Dovato</td>
<td>DTG / FTC A1</td>
</tr>
<tr>
<td>Prezista</td>
<td>DRV 800 mg</td>
</tr>
<tr>
<td>Norvir</td>
<td>RTV C1</td>
</tr>
<tr>
<td>Isentress</td>
<td>FTC / TAF C1</td>
</tr>
</tbody>
</table>

**If viral load is less than 100,000 copies/mL and CD4 count is more than 200 cells/mm³**
Looking ahead
What’s on the horizon—new drugs in development

RECENTLY APPROVED
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 page 31.

PHASE 3
islatravir/3TC/doravirine
Fixed-dose combination of the NNRTI doravirine plus generic 3TC and NRTI islatravir (EfDa). From Merck. On partial clinical hold (see sidebar).

islatravir/doravirine
Dual FDC with NNRTI doravirine. From Merck. On clinical hold (see sidebar).

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. On full and partial clinical hold (see sidebar).

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. Submitted for approval in U.S. in July 2021 (see page 32). On clinical hold (see sidebar).

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.

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

GS-9883
Long-acting formulation of the integrase inhibitor bictegravir. From Gilead.


ALSO SEE HIV life cycle on page 12.
Investigational new drugs

BY MELANIE THOMPSON

At the end of 2021, clinical trials of two promising agents screeched to a halt, disappointing many who were excited about the prospects for long-acting HIV treatment and prevention with islatravir and injectable lenacapavir. This is why we do clinical trials, though, and they did their jobs correctly. Shout out also to independent Data Monitoring Committees.

On November 16, Merck stopped its study of once weekly oral islatravir and MK-8507, an investigational long-acting NNRTI, because the external Data Monitoring Committee (eDMC) detected a decrease in total lymphocytes and T cell counts with the combination. At the time, the changes seemed to be related to the dose of MK-8507. The next week, Merck and Gilead temporarily paused enrollment into the much-anticipated trial of once-weekly oral islatravir and lenacapavir. On December 6, at the recommendation of its eDMC, Merck paused enrollment in its two IMPower trials of once-monthly oral islatravir for PrEP. Just a week later, the FDA placed a partial clinical hold on seven oral islatravir/doravirine trials (no new enrollment, but existing participants continue to get medication) and a complete hold on six other islatravir treatment and prevention trials, including oral, injectable, and implant formulations. At the same time, Merck and Gilead also stopped dosing in a study of oral islatravir and lenacapavir. This may not portend the death of islatravir, but it is too soon to tell.

Lenacapavir, Gilead’s first-in-class capsid inhibitor, was being studied for treatment and prevention via subcutaneous injection every 6 months. Obviously, it needed a suitable partner for treatment, and islatravir appeared to be an excellent choice. Gilead quickly submitted a New Drug Application for lenacapavir based on promising 26-week results of the phase 2/3 CAPELLA trial in heavily treatment-experienced patients with multidrug resistant virus. As with the pivotal trial of fostemsavir, the primary endpoint was change in HIV RNA after 14 days of functional monotherapy, followed by optimization of the background therapy (OBT) and open label lenacapavir. There was also a separate nonrandomized cohort who started LEN and OBT from Day 1. These data were presented last July at the IAS Conference. The combination of injectable lenacapavir and an injectable version of islatravir was on the horizon until the FDA hold on islatravir stopped the phase I trial of the injectable formulation.

For an even worse end to 2021, on December 21, Gilead announced that the FDA had placed a clinical hold on injectable lenacapavir in all ongoing studies for treatment and prevention, due to concerns about the safety of the borosilicate glass vials. Both enrollment and dosing were stopped in 10 ongoing trials. If there is good news here, it is that there was no concern expressed about lenacapavir itself, so one hopes that Gilead will quickly solve this problem and continue on with the trials. However, if problems with islatravir are not solved, it will also be a setback for lenacapavir and LEN will be looking for another date to the prom.

Still in the pipeline are ViiV’s maturation inhibitor GSK-3640254 (called GSK-254); albuvirtide, a fusion inhibitor being developed by Frontier Biotechnologies; and a host of broadly neutralizing antibodies (bnAbs) being studied alone and in combinations for treatment, prevention, and cure. It’s clear that 2022 will be an interesting year in HIV drug development. Get your popcorn!
In this guide, HIV drugs are grouped into nine categories—plus, additional categories for select non-HIV drugs and PrEP.

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<td>Biktarvy</td>
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<td>bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF)</td>
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<td>Cabenuva</td>
<td>LA</td>
<td>cabotegravir/rilpivirine long-acting (CAB LA/RPV LA) injectable</td>
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<td>Cimduo</td>
<td>NRTI</td>
<td>lamivudine/tenofovir DF (3TC/TDF)</td>
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<td>STR</td>
<td>rilpivirine/emtricitabine/tenofovir DF (RPV/FTC/TAF)</td>
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<td>Delstrigo</td>
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<td>doravirine/lamivudine/tenofovir DF (DOR/3TC/TDF)</td>
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<td>Edurant</td>
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<td>elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (EVG/CObI/FTC/TAF)</td>
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<td>Isentress HD</td>
<td>INSTI</td>
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<td>32</td>
<td>Lenacapavir</td>
<td>CAI</td>
<td>lenacapavir (LEN)—NOT YET APPROVED AT PRESS TIME</td>
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<td>Juluca</td>
<td>STR</td>
<td>dolutegravir/rilpivirine (DTG/RPV)</td>
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<td>Norvir</td>
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<td>ritonavir (RTV)</td>
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<td>Odefsey</td>
<td>STR</td>
<td>rilpivirine/emtricitabine/tenofovir alafenamide (RPV/FTC/TAF)</td>
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<td>Pifelatro</td>
<td>NRTI</td>
<td>doravirine (DOR)</td>
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<td>Prezobix</td>
<td>PI/PKE</td>
<td>darunavir/cobicistat (DRV/CObI)</td>
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<td>Prezista</td>
<td>PI</td>
<td>darunavir (DRV)</td>
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<td>Reyataz</td>
<td>PI</td>
<td>atazanavir sulfate (ATV)</td>
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<td>Rukobia</td>
<td>AT</td>
<td>fostemsavir (FTR)</td>
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<td>51</td>
<td>Selzentry</td>
<td>EI</td>
<td>maraviroc (MVC)</td>
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<td>27</td>
<td>Stribild</td>
<td>STR</td>
<td>elvitegravir/cobicistat/emtricitabine/tenofovir DF (EVG/CObI/FTC/TDF)</td>
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<td>Sustiva</td>
<td>NRTI</td>
<td>efavirenz (EFV)</td>
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<td>Symfi/Symfi Lo</td>
<td>STR</td>
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<td>Symtuza</td>
<td>STR</td>
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<td>Temixys</td>
<td>NRTI</td>
<td>lamivudine/tenofovir DF (3TC/TDF)</td>
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<td>Tivicay</td>
<td>INSTI</td>
<td>dolutegravir (DTG)</td>
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<td>Triumeq</td>
<td>STR</td>
<td>dolutegravir/abacavir/lamivudine (DTG/ABC/3TC)</td>
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<td>52</td>
<td>Trogarzo</td>
<td>EI</td>
<td>ibalizumab-uiyk (IBA)</td>
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<td>40</td>
<td>Truvada</td>
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<td>Tybost</td>
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<td>Viread</td>
<td>NRTI</td>
<td>tenofovir disoproxil fumarate (tenofovir DF, or TDF)</td>
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<td>46</td>
<td>Ziagen</td>
<td>NRTI</td>
<td>abacavir sulfate (ABC)</td>
</tr>
</tbody>
</table>

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

**HIV PREVENTION**

<table>
<thead>
<tr>
<th>PAGE</th>
<th>BRAND NAME</th>
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<tbody>
<tr>
<td>57</td>
<td>Apretude for PrEP</td>
<td>PrEP</td>
<td>cabotegravir extended-release injectable suspension (CAB LA)</td>
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<td>58</td>
<td>Descovy for PrEP</td>
<td>PrEP</td>
<td>emtricitabine/tenofovir alafenamide (FTC/TAF)</td>
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<tr>
<td>59</td>
<td>Truvada for PrEP</td>
<td>PrEP</td>
<td>emtricitabine/tenofovir DF (FTC/TDF)</td>
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**NON-HIV DRUGS**

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<tr>
<td>60</td>
<td>Egrifta SV</td>
<td>tesamorelin for injection</td>
<td>for HIV-related hard belly fat</td>
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<tr>
<td>60</td>
<td>Mytesi</td>
<td>crofelemer</td>
<td>for HIV/AIDS-associated diarrhea</td>
</tr>
<tr>
<td>61</td>
<td>Serostim</td>
<td>somatropin for injection</td>
<td>for HIV-related wasting</td>
</tr>
</tbody>
</table>
Biktarvy

bicitravin/emtricitabine/tenofovir alafenamide
BIC/FTC/TAF

Single-tablet regimen containing an INSTI and two NRTIs

Recommended initial regimen for most people

**STANDARD DOSE**
One tablet once daily without regard to food for people taking HIV treatment for the first time (treatment-naive) 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: bicitravin, emtricitabine, or tenofovir. Tablet contains 50 mg of the INSTI bicitravin plus 200 mg emtricitabine and 25 mg TAF.

For adults and children weighing at least 55 pounds (25 kg), use standard dose above or see package labeling. New pediatric formulation available for children at least 2 years old and weighing 30.8–55 pounds (14–25 kg), Biktarvy Low Dose—use one tablet daily with or without food. Each Biktarvy Low Dose tablet contains BIC 30 mg/FTC 120 mg/TAF 15 mg. 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. Biktarvy may be used for people with an undetectable viral load and CrCl less than 15 mL/min who are also receiving hemodialysis.

➤ SEE ALSO DESCovy, which is contained in this drug (bicitravin 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 (rarely experienced) include headache, nausea, and diarrhea. INSTIs and TAF are associated with weight gain. Serum creatinine, estimated creatinine clearance, urine glucose, and urine protein should be obtained before initiating Biktarvy and should be monitored. BIC 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 with INSTIs, primarily among people with a history of psychiatric illnesses. DHHS guidelines recommend closely monitoring people with pre-existing psychiatric conditions. Prior to the initiation of treatment, test for hepatitis B virus (HBV). Severe exacerbations of HBV have been reported in people with co-infection who have discontinued Biktarvy (due to elimination of the emtricitabine and TAF components, which also treat HBV). Monitor liver enzymes closely. Initiation of HBV therapy may be warranted upon discontinuation of Biktarvy. Call your health care provider right away if you develop any of the following signs 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 dofetilide. Not recommended to be taken with Cimduo or Tenioux, Descovy, Emtriva, Epivir-HBV, Hyper, Truvada, Viread, 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, 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 Eclusa, Harvoni, or Vosevi. Tell your provider or pharmacist about all medications, herbas, 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**
New pediatric formulation, Biktarvy Low Dose, became available late last year. Biktarvy is widely prescribed because of its efficacy and safety profile as well as relative lack of resistance emerging from use of this treatment in clinical trials. Data are 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). At this time, there aren’t sufficient data to support the use of Biktarvy during pregnancy. Pregnant women can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; go to apiregistry.com.

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

**AVERAGE WHOLESALE PRICE**
$4,300.56/month

Dr. Melanie Thompson:
Small and potent, Biktarvy is a popular “go-to” initial therapy, including for same-day HIV treatment start. It has a high resistance barrier. A recent randomized open label study, GS-580-4030, found that individuals with suppressed virus on DTG + TDF/FTC or TAF/FTC could safely switch to Biktarvy even in the presence of some previous NRTI resistance, including the M184V mutation associated with resistance to FTC and TDF. Weight gain was associated with more weight gain than elvitegravir/CQIB, NNRTIs, and PIs in several studies. In an analysis of 8 randomized trials, the average weight gain for BIC- and DTG-containing regimens was 3.5 kg (7.7 lbs.) at 96 weeks. It’s important to watch your diet and exercise regardless of what you are taking, but that can be especially true with a TAF + INSTI combo. All INSTIs have the potential for insomnia or, rarely, worsening of depression or suicidal ideation, particularly if there are pre-existing mental health issues. INSTIs have fewer drug-drug interactions than most NNRTIs and PIs. A Gilead-sponsored chart review study in 350 persons who were at least 50 years old who had switched to Biktarvy found that 140 drug interactions in 121 people were avoided by the switch, addressing a common polypharmacy issue in older persons who have multiple comorbidities. Never take Biktarvy with dofetilide, a heart rhythm medicine, as levels of dofetilide are increased and serious rhythm disturbances could occur. Biktarvy increases metformin levels and the metformin dose may need to be adjusted if there are side effects. Several medications for seizures or tuberculosis cannot be taken with Biktarvy. St. John’s wort decreases Biktarvy levels and should be avoided. Take aluminum- or magnesium-containing supplements, vitamins, or antacids at least 2 hours after or 6 hours before Biktarvy, although iron- and calcium-containing compounds can be taken with Biktarvy and a meal. I have seen lots of “low-level viremia” cured by adjusting supplements. Don’t take Biktarvy if you are planning to become pregnant because of lack of data for safety in pregnancy. If you are already pregnant and taking Biktarvy, talk with your HIV care provider about whether it’s advisable to continue the drug.

Activist Michael Broder:
Most people taking Biktarvy (approved in 2018) have no side effects. Concerns have emerged about weight gain on INSTI-containing regimens. As always, your provider should help you weigh the benefits against the risks.
**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 30 mL/min) due to lamivudine component, or those with mild, moderate, or severe liver impairment due to abacavir component. This medication combination, however, is often used in reduced renal function below 30 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.

**SIDES EFFECTS AND TOXICITY**

The most common side effects include insomnia, headache, and fatigue. Data associate INSTIs with weight gain. The pediatric ODYSSEY/PENTA-29 trial reported this year did not observe the weight gain seen in adults. DTG can cause a small, reversible increase in serum creatinine within the first few weeks of treatment, but does not affect actual kidney function. Serum creatinine within the first few weeks of treatment, but does not affect actual kidney function. Monitor liver enzymes closely. Initiation of HBV therapy may be warranted upon discontinuation of Triumeq. Call your health care provider right away if you develop any of the following signs 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 doxifluridine. Triumeq should be taken two hours before or six hours after taking antacids or laxatives, 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, Nexum, Pepsid, Prevacid, Prilosec, and Zantac) are okay to use. Avoid co-administration with oxicarbazepine, 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). May increase levels of dalfampridine, which may increase the risk of seizures. When taking carbamazepine or rifampin, take an additional dose of DTG (in the form of one Tivicay tablet) 50 mg 12 hours after taking Triumeq's dose. Tell your provider or pharmacist about all medications, herbs, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions that are not listed here.

**MANUFACTURER**

Viiv Healthcare

viivhealthcare.com; triumeq.com

(877) 844-8972

**AVERAGE WHOLESALE PRICE**

$4,006.67/month
**Dovato**

**dolutegravir/lamivudine**

**DTG/3TC**

**Single-tablet regimen containing an INSTI and an NRTI**

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-naive 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 (now down to a creatinine clearance less than 30 mL/min) due to the lamivudine component. This medication combination, however, is often used in reduced renal function below 30 mL/min due to the relatively minimal risk of lamivudine accumulation and side effects. In addition, reduced doses may be obtained by using the individual components of this medication as needed.

**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, Eplusaha, 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, herbs, 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 Epivir). Dolutegravir is from a 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, minimizing the potential for side effects. At one, two, and nearly three years into 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 two-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. 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-53 of perinatal guidelines at hivinfo.nih.gov. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

**MANUFACTURER**

ViiV Healthcare

vivihc.com; dovato.com;

(877) 844-8872

**AVERAGE WHOLESALE PRICE**

$3,182.63/month

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**STAFF Pick:**

Dovato (due to elimination of the TAF-based regimen can switch to DTG/3TC and maintain viral suppression. Weight gain with dolutegravir remains a concern, as well as the other possible INSTI side effects (insomnia, new or worsening depression). Drug interactions of note include increases in the levels of dofetilide (which is contraindicated), metformin, and some other drugs. Concerns have decreased regarding serious birth defects (specifically neural tube defects) in infants when dolutegravir is taken at the time of conception. The very small and not statistically significant risk should be discussed with persons of childbearing potential who are starting Dovato. For more information on dolutegravir, see the discussion of Tivicay.

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**ACTIVIST MICHAEL BRODER:**

Dovato (approved in 2019) should not be taken by people with a viral load greater than 500,000 copies, or by people with hepatitis B virus (HBV) co-infection. Concerns have emerged about weight gain on INSTI-containing regimens. As always, your provider should help you weigh the benefits against the risks.
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 six 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 doses 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. Data associate INSTIs with weight gain. 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 with INSTIs, primarily in people with a history of psychiatric illnesses. DHHS guidelines recommend closely monitoring anyone with pre-existing psychiatric conditions. 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 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 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). Juluca should not be taken with proton pump inhibitors (such as AcipHex, Deslantil, Prilosec, Prevacid, Protonix, Nexium). Avoid taking Juluca with some seizure medicines (carbamazepine, oxcarbazepine, phenobarbital, and phe- nytoin) 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, herbas, 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. Juluca still works against two stages of the virus life cycle, as do the three-drug regimens. The guidelines cite Juluca as “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 smallest STR, which might be advantageous in 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. Rifampirine is an alternative drug for use during pregnancy, and although dolutegravir is now a preferred medication in pregnancy as well as for people who are trying to conceive, U.S. HIV perinatal treatment guidelines suggest using three-drug regimens. Find the discussion on page C-53 of perinatal guidelines at hivinfo.nih.gov. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO aregistry.com.

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

AVERAGE WHOLESALE PRICE
$3,755.30/month

DR. MELANIE THOMPSON:
Not approved for initial therapy, Juluca is a nuke-sparing two-drug regimen for maintenance of viral suppression in people who are doing well on their current regimen. Because it does not contain any drugs active against hepatitis B, you shouldn’t go on Juluca if you have hepatitis B.

Weight gain, rash, insomnia, liver toxicity, and new or worsening depression have been noted with components of Juluca. Diarrhea and headache were the most common side effects in the SWORD clinical trials. Creatinine increased by about 0.1 mg/dL in SWORD, but this was due to changes in kidney secretion of the drugs, not kidney toxicity. Juluca cannot be taken with dofetilide and some medications for seizures and tuberculoses. In addition, St. John’s wort, dexamethasone, and acid blockers should be avoided as they decrease levels of rilpivirine, dolutegravir, or both. Metformin levels are increased by dolutegravir and may need to be adjusted, and should be limited to 1,000 mg/day. Juluca should be taken 4 hours before or 6 hours after taking sulfa/urate or aluminum- or magnesium-containing supplements or medications, or if taking calcium- or iron-containing products on an empty stomach. Calcium and iron can be taken with Juluca if taken with a meal.

Concerns about birth defects with dolutegravir have greatly diminished, but should be discussed with an HIV care provider (see Tivicay).

There is speculation that Juluca might be used as a bridging drug if doses of Cabenuva have to be missed, due to the similarities between dolutegravir and cabotegravir. This has not been studied in clinical trials. Oral cabotegravir and rilpivirine are supplied by ViiV at no cost for persons on Cabenuva.

For more information about Juluca, see comments on Tivicay and Edurant.

ACTIVIST MICHAEL BRODER:
Approved in 2017, Juluca was the first two-drug STR. Getting a two-drug STR into clinical use was a big deal. But there are downsides. First off, Juluca is for use only by people who have been undetectable on another regimen for at least six months, not for first-time treatment. People with HIV and HBV co-infection should not take Juluca, because neither dolutegravir nor rilpivirine treats HBV. The rilpivirine component has significant drug-drug interactions, and needs to be taken with food (at least 400 calories). Two years after launching Juluca, drugmaker ViiV got approval for Dovato, which kept the dolutegravir component, but replaced the rilpivirine with the NRTI lamivudine—a two-drug regimen that is among those recommendedit for initial treatment. If your provider recommends Juluca, they may have a good reason, but ask them what it is.
Darunavir, boosted by 150 mg cobicistat, with 200 mg emtricitabine

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 sub-
stantial lower exposures of darunavir and cobicistat components during pregnancy.

Positively Aware 2022 HIV Drug Guide

Symtuza darunavir/cobicistat/emtricitabine/tenofovir alafenamide

DRV/COBI/FTC/TAF

Single-tablet regimen containing a protease inhibitor, a pharmacokinetic enhancer (booster), and two NRTIs

Recommended initial regimen in certain clinical situations

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

Darunavir contains a sulfa component, so use with caution in people 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. Data associate TAF with weight gain. Observational cohort studies reported an asso-
ciation between some PIs (including darunavir taken with ritonavir) and an increased risk of cardiovascular (CV) events. Data on darunavir plus cobicistat are too limited to be substantiated, so use with caution in individuals with suppressed viral load on a stable HIV regimen for more information. While cobicistat increases estimated creatinine clearance, its effect on SCr can make monitoring of impaired kidney function more difficult or less accurate. Monitoring of impaired kidney function should be closely monitored for renal safety. Serum phosphorus in people with or at risk for kidney impairment should also be monitored. Prior to initiation, people should be tested for hepati-

Symtuza is the first STR containing a protease inhibitor. This formulation is much more conve-

vant and reduces the number of pill co-pays to one. It is not the same as Prezobix plus Descovy, because Symtuza contains a lower dose of TAF than Descovy. A benefit of the PIs is their high genetic barrier to developing drug resistance. While medical providers may hate to say it out loud, this means greater for-
giveness 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 treat-

ment. In fact, the FDA allowed Janssen to advertise Symtuza as “help[s] protect against resistance.”

Potential Drug Interactions

Do not take with alfuzosin, carbam-

azepine, dexamethasone, dronedar-

one, ergot derivatives, ivabradine, oxcarbazepine, pimozide, primidone, pro-
vitamin A, salmeterol, ticagrelor, trimcinolone, or voriconazole. Beclometasone, prednisolone, and prednisone are not recommended to be taken with avana-
f, ciclesonide, dabigatran etexilate (in renal impairment), everolimus, Intenitol, irinotecan, mometasone, rifabutin, rifampin, rivaroxaban, salmeterol, ticagrelor, trimcinolone, or voriconazole. Beclometasone, prednisolone, and prednisone are not recommended to be taken with avana-

ative of Symtuza, talk with your HIV care provider about whether you should continue the drug.

Potential Interactions

Drug-drug interactions that are not listed here.

Recommended initial regimen in certain clinical situations

Symtuza is the first 4-drug STR and the most expensive of regimens for initial therapy at a wholesale acquisition cost of $4,065 per month. It is not recommended for initial therapy for most people because of all of the drug-drug interactions that COBI brings to the table. A rel-
avely small, open label study of Symtuza for rapid ART (antiretroviral therapy) initiation found high levels of viral suppression and low drug-related side effects, but there are other drug interactions that setting for people who cannot take the recommended INSTI regimens. Darunavir has a high genetic barrier to resistance. A large observational study found an association between daruna-

vir and cardiovascular disease. Symtuza is not recommended in pregnancy because of lower levels of cobicistat and also darunavir in the second and third trimesters can decrease antiviral efficacy. If you are pregnant and must continue Symtuza, talk with your health care provider right away if you develop any of the following signs or symptoms of hepatitis: yel-

lobing 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.

Activist Michael Broder: Back in the day, darunavir was touted for its high genetic barrier to resistance. But given newer options, nobody these days needs to be on a boosted anything. Cobicistat increases levels of darunavir by inhibiting an enzyme pathway in the liver. Problem is, it also boosts levels of other medications a person may be taking, and that can be a problem.

Atazanavir (the only other PI on the market). Darunavir regimens have an AI rating from DHHS (“A” for strong) vs. the Roman numeral “I” for “data from randomized controlled trials”) vs. a BI rating for atazanavir (“B” for “Moderate”).

Patient groups can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apiregistry.com.

Manufacturer

Janssen Therapeutics

Average Wholesale Price

$15,150.92/month
**STANDARD DOSE**

One tablet once daily without regard to food for people taking HIV treatment for the first time (treatment-naive) 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%), nervousness, 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 (for example, 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 (for example, lethargy, drowsiness, etc.) was associated with 4% of people in the Delstrigo group compared to 6% of those on Atripla. Dizziness could be signs of 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 HBV 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 HBV 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, Epivir, or Viread, all used for hepatitis B. When using with the antibiotic drug rifabutin (used for TB and to decrease in CD4 count, doravirine should not be used with Delstrigo: the anticonvulsants carbamazepine, oxcarbazepine, phenobarbital, and phenytoin; the androgen receptor inhibitor enzalutamide; the anticytotoxic antibiotics rifampin and rifapentine; the cytotoxic agent (a cancer drug) mitotane; and the herbal St. John’s wort. Avoid using sorbitol-containing medicines with lamivudine; there may be an increased risk of 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, herbal, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions that are not listed here.

**MORE INFORMATION**

Stand-alone versions of doravirine (Pifeltro) and lamivudine/tenofovirdisoproxil fumarate (Cimduo, Temixys) are also approved; see those pages. Delstrigo contains an older prodrug of tenofovir, TDF. A safer version, TAF, is available and used in some STRs. However, as TAF and INSTIs may have some association with weight gain, Delstrigo may become a more popular option. According to a new DHHS statement last year, “In a cross-trial analysis, DOR was not associated with weight gain compared with [efavirenz] 600 mg or boosted [darunavir].” 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 such clinical trials yet. In the DRIVE-FORWARD study comparing doravirine to darunavir, at 96 weeks, 72% of treatment-naive individuals in the doravirine group attained undetectable status (a viral load of less than 50 copies/mL), compared to 65% for the darunavir group. 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 safety use of Delstrigo during pregnancy. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

**MANUFACTURER**

Merck & Co.

**DR. MELANIE THOMPSON:**

Delstrigo is the first STR to be coformulated with a newly approved drug and two drugs that are generic, allowing for a lower average wholesale cost of $2,315 per month. You would expect it to be lower than it is, though, wouldn’t you? Doravirine was well tolerated in clinical trials, with fewer neuropsychiatric side effects than efavirenz, in the DRIVE-AHEAD trial, and less diarrhea and nausea than ritonavir-boosted darunavir, based on DRIVE-FORWARD. Lipid changes were lower with the doravirine regimen in both trials. Kidney and bone density effects of TDF are key considerations in terms of side effects (see Viread). In a cross-study analysis, mean weight gain with doravirine (0.7 kg—that is, 3.74 lbs.) was more than with efavirenz (0.6 kg) and similar to that with ritonavir-boosted darunavir (1.4 kg) at 48 weeks, but all were similar at week 96.

**ACTIVIST MICHAEL BRODER:**

TDF, notorious for safety issues with bones and kidneys, has been kicked aside by its safer chemical cousin, tenofovir alafenamide (TAF). If your provider recommends Delstrigo, they may have a good reason, but make sure they tell you what it is.
STANDARD DOSE (FOR BOTH GENVOYA AND STRIBILD)
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 the regimen. Tablets contain 150 mg of the INSTI elvitegravir boosted by 150 mg cobicistat plus 200 mg emtricitabine, with 10 mg TAF in Genvoya and 300 mg TDF in Stribild.

GENVOYA: 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. Dose cannot be adjusted for people with liver problems. Genvoya is not recommended for people who have severe liver problems, a CrCl between 15–30 mL/min, or a CrCl less than 15 mL/min who are not receiving chronic hemodialysis.

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

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: Emtriva, Viread, 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 include nausea and diarrhea. INSTIs and TAF have been associated with weight gain. Cobicistat can cause a small, reversible increase in serum creatinine with no known effect on actual kidney function. 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 people 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 HBV have been reported in people co-infected with HBV who have discontinued Genvoya or Stribild (due to elimination of the emtricitabine and tenofovir components, which also treat hepatitis B). Monitor liver enzymes closely in co-infection. HBV therapy may be warranted upon discontinuation. Call your health care provider right away if you develop any of the following signs 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.

Before taking Genvoya or Stribild, 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 or Stribild.

POTENTIAL DRUG INTERACTIONS
Do not take with Cimexor or Temixys, Descovy, Emtriva, Epivir-HBV, Hepsera, Truvada, Vemlidy, or Viread. 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 lovastatin or simvastatin, afluzosin, carbamazepine, phenobarbital, phenytoin, ergotamine, dihydroergotamine, methyl-ethyl-ergolide, midazolam, lurasidone, pimozide, Revatio, rifampin, rifabutin, rifapentine, Serevent, triazolam, St. John’s wort, clopidogrel, or ticagrelor. Rosuvastatin and atorvastatin should be used with caution and started at the lowest effective dose possible. Monitor closely for increased side effects, such as muscle pain, from these medications. An alternative corticosteroid to systemic dexamethasone should be considered. Risks versus benefits of use in patients with voriconazole should be assessed with expert consultation. Concentrations of antidepressants such as fluoxetine, paroxetine, bupropion, or amitriptyline may be increased, and their doses may need to be reduced. Levels of many nasal and inhaled steroids like fluticasone may be increased, which may lead to symptoms of Cushing’s syndrome. An alternative corticosteroid 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 a low dose and titrate based on tolerability and clinical effect. Reduce Daklinza dose to 30 mg. Taking with Olysio, Viekira Pak, or Zepatier is not recommended. Tell your provider or pharmacist about all medications, herbal medicines, and supplements you are taking or thinking of taking, prescribed or not, as there are many other drug interactions not listed here.

GENVOYA: Dose of clarithromycin may need to be reduced based on kidney function. Can be taken with Harvoni or Epclusa.

STRIIBILD: No significant interactions with beclomethasone or prednisolone. Use caution with beta blockers and calcium channel blockers. Co-administer bosentan and immunosuppressants such as Prograf, Gengraf, Neoral, and Sandimmune with caution. Taking with Harvoni, Olysio, Viekira Pak, or Zepatier is not recommended. Monitor kidney function more closely with Epclusa.

MORE INFORMATION
Genvoya and Stribild are not recommended during pregnancy. Switching regimens should be considered for anyone who is pregnant. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO aregistry.com.

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

GENVOYA AWP $4,300.56/month
STRIIBILD AWP $4,511.29/month
STANDARD DOSE (FOR BOTH ODEFSEY AND COMPLERA)
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 tenofovir. Tablet contains 25 mg of the NNRTI rilpivirine plus 200 mg emtricitabine and 25 mg TAF in Odefsey or 300 mg TDF in Complera.

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 for Odefsey or 50 mL for Complera. Odefsey should be used with caution in adults with end-stage renal disease (ESRD) with an estimated CrCl below 15 mL/min who are receiving chronic hemodialysis (HD). Take the Odefsey dose after completion of dialysis. Complera should not be used in people with CrCl less than 50 mL/min or severe liver impairment.

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/mm³ before taking rilpivirine. Prior to initiation, people should be tested for hepatitis B infection. HBV reactivation has been reported with regimens containing rilpivirine because these drugs increase rilpivirine levels, which can increase the risk of side effects. Reduced methadone levels can occur; while dose adjustments are not necessary, it is recommended to monitor for withdrawal symptoms. Taking Odefsey with rifabutin is not recommended. Co-administration of rifabutin with Complera requires an extra Edurant tablet in addition to Complera. 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 and Truvada, but monitor for tenofovir toxicity with Complera. Tell your provider or pharmacist about all medications, heartburn or stomach acid drugs such as Pepcid, Tagamet, and Zantac can be taken 12 hours before or four hours after a dose of Odefsey or Complera.

In co-infection, initiation of HBV 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, achiness, or tenderness on the right side below the ribs. See Descovy page for more possible effects on kidney function with Odefsey. Increased monitoring for adverse events is recommended for people with ESRD who are taking Odefsey. See Viread for TDF in Complera. See Truvada page for other possible effects on kidney function.

POTENTIAL DRUG INTERACTIONS
Do not take with Cimduo or Temixys, Descovy, Emtriva, Epivir-HBV, or Truvada, which are all used for the treatment of hepatitis B. Proton pump inhibitors (PPIs), which lower stomach acid, such as Aciphex, Dexiant, Nexium, Prevacid, Prilosec, Protonix, or Veloca cannot be taken with Odefsey or Viread, which are all used for the treatment of hepatitis B. Monitor liver enzymes closely in co-infection. Initiation of HBV 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, achiness, or tenderness on the right side below the ribs. See Descovy page for more possible effects on kidney function with Odefsey. Increased monitoring for adverse events is recommended for people with ESRD who are taking Odefsey. See Viread for TDF in Complera. See Truvada page for other possible effects on kidney function.

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 observed. Cases of rash, angioedema (swelling), urticaria (itchy rash), and increased liver enzymes have also been reported with regimens containing rilpivirine. TAF has been associated with potential weight gain. There may be a small increase in serum creatinine (SCr) and decrease in estimated creatinine clearance (CrCl) associated with rilpivirine. Prior to initiation, people should be tested for hepatitis B virus (HBV) infection. Severe exacerbations of HBV have been reported in people co-infected with HBV who have discontinued Odefsey or Complera (due to elimination of the emtricitabine, TAF, and TDF components, which also treat hepatitis B). Monitor liver enzymes closely in co-infection. Initiation of HBV 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, achiness, or tenderness on the right side below the ribs. See Descovy page for more possible effects on kidney function with Odefsey. Increased monitoring for adverse events is recommended for people with ESRD who are taking Odefsey. See Viread for TDF in Complera. See Truvada page for other possible effects on kidney function.

SEE THE INDIVIDUAL DRUGS:
Edurant, Descovy (coformulation of Emtriva and TAF), or Truvida (coformulation of Emtriva and TDF).

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

SEE THE INDIVIDUAL DRUGS:
Edurant, Descovy (coformulation of Emtriva and TAF), or Truvada (coformulation of Emtriva and TDF).

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

Recommended initial regimens in certain clinical situations

DR. MELANIE THOMPSON:
These STRs differ only in the use of TAF (Odefsey) or TDF (Complera). They are no longer recommended as initial therapy in most people, largely because of potency and drug interactions. Studies showed worse response when used as initial treatment in persons with viral load greater than 100,000 copies/mL and CD4 counts ≤ 200 cells/L, so they are not recommended in this population and they certainly are not to be used for rapid start of HIV treatment. They have fewer CNS side effects than Atripla but still can be associated with depression in some people, and can exacerbate pre-existing depression. Elevation in lipids is less than with efavirenz and rash is infrequent but can also occur, along with a severe hypersensitivity reaction. The choice between the drugs should be made based on the side effects of TAF (elevation in both HDL and LDL cholesterol and possible weight gain) and TDF (risk of kidney impairment and loss of bone density). See Descovy and Truvada for more information.

ACTIVIST MICHAEL BRODER:
Due to the relatively poor performance of rilpivirine among people with higher viral loads in clinical trials, Odefsey and Complera can be used for initial therapy only by people with a viral load less than 100,000 copies/mL. They need to be taken with food (at least 400 calories) to ensure adequate absorption of rilpivirine. Given other available options, it’s hard to imagine why any provider nowadays would recommend Odefsey or Complera.

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

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

ODEFSEY AWP
$3,913.84/month

COMPLERA AWP
$3,913.84/month

Odefsey
rilpivirine/emtricitabine/ tenofovir alafenamide
RPV/FTC/TAF

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

Single-tablet regimens containing an NNRTI and two NRTIs

MANUFACTURERS:
Gilead Sciences, Inc.
gilead.com; genova.com
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Janssen Therapeutics
janssentherapeutics.com
(800) JANSSEN (526-7736)

ODEFSEY AWP
$3,913.84/month

COMPLERA AWP
$3,913.84/month


**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 50 mL/min or individuals requiring dialysis. Similar, but not exact, medications are available (see Symfi and Symfi Lo).

**POTENTIAL SIDE EFFECTS AND TOXICITY**

Use with caution in individuals with depression or other psychiatric issues, and those 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 people 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. TDF is associated with long-term decreases in bone mineral density (BMD); see Viread. 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). Severe exacerbations of HBV have been reported in people co-infected with HBV who have discontinued Atripla (due to elimination of the emtricitabine and TDF components, which also treat HBV). Monitor liver function in people with coinfection. Initiation of HBV therapy may be warranted upon discontinuation of Atripla. 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. Efavirenz 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 recently pregnant individuals with HIV who are taking a regimen containing efavirenz. Efavirenz can cause a false positive result for marijuana on certain drug tests. A more specific confirmatory test can be done.

**POTENTIAL DRUG INTERACTIONS**

Do not take with Cimduo or Temixus, Descovy, Emtriva, Epivir-HBV, Hespera, Truvada, Vemivid, or Viread. Other antiretrovirals may interact with efavirenz or ritonavir. Note: Efavirenz, ritonavir, and irtraconazole, ergot derivatives, midazolam, pimozone, 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 people 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 also be required for 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. No 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 necessary when using 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 for 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 Eplulsa or Zepeptar. Not intended to be taken with other HIV medications, unless prescribed that way. Tell your provider or pharmacist about all medications, herbs, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions that are not listed here.

**MORE INFORMATION**

Check with your provider or pharmacist first before stopping Atripla, so that you avoid the rapid development of HIV resistance to it. A genetic trait affecting drug metabolism of efavirenz leading to a higher rate of side effects, occurs more in African Americans. 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 it. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; go to apregnancy.com.

**MANUFACTURERS**

Bristol-Myers Squibb (800) 321-1335

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

**AVERAGE WHOLESALE PRICE**

Generic is available: $3,413.97/month

**ACTIVIST MICHAEL BRODER:**

Given newer options, Atripla (approved in 2006) has two strikes against it: efavirenz and TDF. Efavirenz breathed new life into the NNRTI class when it was on life support in the wake of bad pharmacology (delavirdine) and bad marketing (nevirapine). But it causes serious neuropsychological side effects such as nightmares, depression, and suicidal ideation that can make it difficult to tolerate. As for TDF, it is effective and tolerable with a great resistance profile. Unfortunately, there are worriesome bone and kidney side effects. Given other available options, it’s hard to imagine why any provider today would recommend Atripla for anyone requiring HIV treatment.

**DR. MELANIE THOMPSON:**

Atripla revolutionized HIV treatment in 2006 when it became the first once-daily STR, but it has not been recommended for initial therapy for most people in the U.S. for a number of years, largely due to its many side effects. Central nervous system side effects include depression, dizziness, sleepiness, abnormal dreams, headache, and most notably, suicidality. Others include rash, elevation of LDL cholesterol, and ERG changes that are serious. It has serious heart rhythm abnormalities (QTc prolongation). Efavirenz also has many drug-drug interactions that complicate its use. The Atripla lookalike generics Symfi and Symfi Lo both use 5TC instead of TDF. It’s unfortunate that HIV generics often only emerge after the usefulness of the drug has passed. This speaks to the complicated and profit-driven game that is drug development in the U.S. but also to the extremely rare rate of drug advances in HIV treatment. See Descovy and Truvada.
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 doses 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 people 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.

POSSIBLE SIDE EFFECTS AND INTERACTIONS
The most common side effects include headache, body pain, fever, abdominal pain, back pain, asthenia (physical weakness or lack of energy), diarrhea, nausea, vomiting, arthralgia (joint pain), depression, insomnia, anxiety, pneumonia, and rash. 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. See Viread for TDF information. 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). Seroconversion rates for HBV after treatment with hepatitis B (HBV) 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, pimozone, triazolam, benridl, or St. John’s wort. Efavirenz should also not be taken with other medications that prolong QTc interval (a heart problem) or medica tions with a known risk for torsades de pointes. For people 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 also increase effectiveness of birth control pills; consider the use of other contraceptive methods. Close 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 medications with lamivudine; there are many, such as aciclovir, abacavir, lic ytid (Teylon liquid and others). 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, herbs, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions that are not listed here.

MORE INFORMATION
Symfi and Symfi Lo are basically alternative versions of Atripla, a medication that’s no longer pref erred 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 efavirenz, 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 efavirenz along with fewer side effects. Be careful when stopping these medications, so that you avoid rapid development of HIV resistance to them. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

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

Dr. Melanie Thompson: Atripla revolutionized HIV treatment in 2006 when it became the first once-daily STR, but it has not been recommended for initial therapy for most people in the U.S. for a number of years, largely due its many side effects. Central nervous system side effects include depression, dizziness, sleepiness, abnormal dreams, headache, and most notably, suicidality. Others include rash, elevation of LDL cholesterol, and EKG changes that could be beneficial. This drug’s advantage is the extremely rapid heart rhythm abnormalities (QTc prolongation). Efavirenz also has many drug-drug interactions that complicate its use with many other drugs. The generics Symfi and Symfi Lo both use 3TC (which is generic instead of FTC), and Symfi Lo uses a 400 mg dose of efavirenz that has been associ-ated with fewer side effects. It’s unfortunate that HIV generics only often emerge after the use-fulness of the drug has passed. This speaks to the complicated and profit-driven game that is drug development in the U.S. but also to the extremely rapid pace of drug advances in HIV treatment.

Activist Michael Broder: Symfi and Symfi Lo were approved in 2018, and are “brand- generic” versions of Atripla. When Atripla was approved, efavirenz and TDF were the “it” drugs (and emtricitabine was virtually a carbon copy of the highly successful lamivudine), and Atripla quickly became the market leader. But efavirenz causes neurologic side effects such as nightmares, depression, and suicidal ideation. As for TDF, it is effective and tolerable with a great resistance profile but has worrisome bone and kidney side effects, and has been supplanted by its safer chemical cousin, TAF. Given other available options, it’s hard to imagine why any provider today would recommend Symfi for anybody. But if your provider recommends Symfi or Symfi Lo, they may have a good reason, but make sure they tell you what it is.
Cabenuva contains an INSTI and an NNRTI

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

Recommended as optimization therapy for people with undetectable HIV viral load for at least 3 months on treatment

STANDARD DOSE
Two long-acting intramuscular gluteal (buttock muscle) injections once every two months. May be taken once monthly. Cabenuva 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, no active hepatitis B infection, and no drug resistance or suspected resistance to cabotegravir or rilpivirine. A month of daily oral lead-in therapy is recommended 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 the oral lead-in. Initiation dose is 600 mg CAB LA plus 900 mg RPV LA (3 mL each). Then for every other month administration, continue with this dose every month thereafter. For monthly dose, continue with a lower maintenance dose of 400 mg CAB LA plus 600 mg RPV LA (2 mL each). Smaller dose may cause less pain or discomfort. See package insert for instructions on using the oral medications during planned or unplanned missed injections (Section 2.8). Oral medication may be taken until injections can be restarted (for both monthly and every other month dose schedule). See Table 4.4 for alternative injection regimens. Increased monitoring is recommended when CrCl is less than 30 mL/min. The effect of severe liver impairment on Cabenuva is unknown. People may be given Cabenuva up to 7 days before or after the date the patient is scheduled to receive monthly or every other month injections. Providers should follow directions for administration (Section 2.9 of package insert). Longer needles (not included in the dosing kit) may be required for people with a BMI (body mass index) greater than 30.

POTENTIAL SIDE EFFECTS AND TOXICITY

Potential side effects and interactions. People given injections should be advised to stretch and remain active. It is strongly discouraged to massage the area. Liver toxicity (hepatotoxicity) has been reported with or without pre-existing liver disease or risk factors. People with underlying liver 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 people with pre-existing psychiatric conditions on an INSTI. Monitor for signs of hypersensitivity, including elevated liver transaminases, and treat as needed. Data associate INSTIs with weight gain. There was an average age at initiation of 3.3 pounds weight gain in Cabenuva trials.

Residual concentrations may remain in the body for more than a year after discontinuation. Therefore, it is essential to initiate a new treatment, fully suppressive regimen no later than one month after the final injection doses of Cabenuva. If virologic failure is suspected, prescribe an alternative regimen as soon as possible. Analyses indicate that having two of the following baseline factors may be associated with an increased risk of virologic failure: archived rilpivirine resistance mutations, HIV-1 subtypes A6/A1, or BMI (body mass index) greater than 30 kg/m². People with a history of exposure to an NNRTI may consider obtaining a GenoSure Archive resistance test to assess archived mutations which may decrease the susceptibility to rilpivirine. Pregnant individuals can voluntarily enroll in the NIHAsure Viral Pregnancy Registry through their provider; GO TO appregistry.com. -

ACTIVIST MICHAEL BRODER: According to surveys most people taking Cabenuva like it, and would not want to go back to daily pills.

AVERAGE WHOLESALE PRICE
28-day oral lead-in provided at no cost
Loading dose (600 mg/900 mg): $7,306.20
 Maintenance dose (400 mg/600 mg): $4,870.80/month

DR. MELANIE THOMPSON: Cabenuva is the first complete injectable regimen for HIV treatment and can be given once every two months. People who hate pills, or are just sick of taking them, and don’t mind injections might be very interested in this regimen, but it’s not for everyone. Injection site reactions are the most common side effect but are generally mild and resolve quickly.

The FAIR study included 111 people who switched from oral DTG/RPV/FTC directly to cabotegravir and rilpivirine (CAB + RPV at week 100 with similar safety and efficacy 24 weeks later. This suggests that a direct-to-injection strategy should be explored in clinical trials. If doses must be missed, a bridging oral regimen should be used. If you are on HIV you provides the oral lead-in and bridging regimens to Cabenuva users at no additional cost. If you are interested in Cabenuva, it is important to consider whether you would be able to get to clinic 24 hours every month or every other month. Levels of the drugs may persist in the body a long time (up to a year or longer), but when they drop below the levels needed to suppress virus, viral resistance to one or both drugs can result, so it is important to attend visits exactly as scheduled. If you are on Cabenuva and you decide that injections are not for you, your HIV care provider right away so you can start oral treatment again at the appropriate time to keep your virus suppressed.

The cost of Cabenuva is extremely high, at a wholesale acquisition cost of $5,940 for the loading initial dose and $3,960 for monthly maintenance doses. This does not include what your care provider’s office charges for administering the drugs, or for office time. Of course, ViV has a patient assistance program that aims to pick up enough of your out-of-pocket drug cost to make Cabenuva feasible while keeping prices very high, but it is really unfortunate that prices remain at this egregious level.

MANUFACTURER
ViV Healthcare
viivhealthcare.com; cabenuva.com (877) 844-8972

SEE EDURANT; cabotegravir is not available separately
SEE PACKAGE INSERT for more complete information on potential side effects and interactions.

MORE INFORMATION
Residual concentrations may remain in the body for more than a year after discontinuation. Therefore, it is essential to initiate a new treatment, fully suppressive regimen no later than one month after the final injection doses of Cabenuva. If virologic failure is suspected, prescribe
Lenacapavir, Gilead’s first-in-class capsid inhibitor, was being studied for treatment and prevention via subcutaneous injection every six months. Obviously, it needed a suitable partner for treatment, and islatravir appeared to be an excellent choice. Gilead quickly submitted a New Drug Application for lenacapavir based on promising 26-week results of the phase 2/3 CAPELLA trial in heavily treatment-experienced people with multidrug-resistant virus. As with the pivotal trial of fos-temsavir (Rukobia), the primary endpoint was change in HIV RNA after 14 days of functional mono-therapy, followed by optimization of the background therapy (OBT) and open label lenacapavir. There was also a separate nonrandomized cohort who started LEN and OB from Day 1. These data were presented at the July 2021 IAS Conference. The combination of injectable lenacapavir and an injectable version of islatravir was on the horizon until the FDA hold on islatravir stopped the phase 1 trial of the injectable formulation. For an even worse end to 2021, Gilead announced that the FDA had placed a clinical hold on injectable lenacapavir in all ongoing studies for treatment and prevention, due to concerns about the safety of the borosilicate glass vials. Both enrollment and dosing were stopped in 10 ongoing trials. If there is good news here, it is that there was no concern expressed about lenacapavir itself, so one hopes that Gilead will quickly solve this problem and continue on with the trials. However, if problems with isla-travir are not solved, it will also be a setback for lenacapavir and LEN will be looking for another date to the prom.

ACTIVIST MICHAEL BRODER: Lenacapavir is an investigational drug, meaning it is still in clinical trials, and not yet approved for clinical use. Lenacapavir is on track to be the first in a new class of HIV drugs called capsid inhibitors. The genetic material of HIV is packaged inside a cone-shaped structure called a capsid, which is made of a protein also called capsid. Lenacapavir interferes with capsid functions at multiple points in the viral life cycle. Lenacapavir is being evaluated for use by people who have been on a number of previous HIV treatment regimens and have multidrug-resistant virus. Based on promising clinical trial results reported last summer, it is possible that lenacapavir will be approved for this indication in the spring of 2022.

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Tivicay, dolutegravir

**INTEGRASE STRAND TRANSFER INHIBITOR**

Recommended as a component of initial regimen for most people

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**STANDARD DOSE**

One 50 mg tablet once daily without regard to food, for individuals on HIV therapy for the first time (treatment-naive) 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. Tivicay PD tablets (5 mg), taken without regard to food 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 children weighing 30.8 up to 44 lbs. Dosing under 44 lbs 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.

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**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 developing resistance, similar to the protease inhibitors (such as Prezista). 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.

Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; go to aregistry.com.

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**POTENTIAL DRUG INTERACTIONS**

It is important to take Tivicay only with other HIV drugs recommended by your provider because it and similar drugs are contained in other HIV medications: Biktarvy, Genvoya, Isentress, Stribild, Truvada, Tivicay, and Juluca. Do not take with the anti-arrhythmic block dalfampridine, which could increase the risk of seizures. No known interactions with Epclusa, Harvoni, or Zepatier. Tell your provider or pharmacist about all medications, herbs, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions that are not listed here.

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**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 (creatinine phosphokinase, a lab value indicating muscle damage), rhabdomyolysis (breakdown of muscle), and myopathy or myositis (muscle pain) were also reported. Data associate INSTIs with weight gain. In findings reported this year, the pediatric ODYSSEY/PENTA-29 Trial did not observe the weight gain seen in adults. There have been rare reports of depression and suicidal ideation, primarily among people with a history of psychiatric illnesses, in people receiving INSTI-based regimens. DHHS guidelines recommend closely monitoring people 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.

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**ADDITIONAL INFORMATION**

For more information, visit positivelyaware.com/tivicay or viivhealthcare.com.

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**SEEN PACKAGE INSERT for complete information on potential side effects and interactions.**

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**MANUFACTURER**

Viiv Healthcare

viivhealthcare.com; tivicay.com

(877) 844-8872

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**AVERAGE WHOLESALE PRICE**

50 mg tablets: $2,413.66/month

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**ACTIVE INGREDIENT**

Dolutegravir (50 mg)

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**SAFE SIDE EFFECTS**

There were 2-3% moderate insomnia, fatigue, and headache in clinical trials, but the vast majority of those on Tivicay had no side effects at all. Concerns have emerged about weight gain on INSTI-based regimens. Your doctor can help you weigh the benefits against the risks.

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**DR. MELANIE THOMPSON:**

Preliminary results from a pregnancy study in Botswana raised concern that dolutegravir might be associated with birth defects, specifically neural tube defects, when taken at the time of conception. Follow up of this study confirmed, however, that the rate of neural tube defects in infants of persons taking DTG at the time of conception was only slightly—and not statistically significantly—higher than in those not on DTG (1.9 v. 1.1 per 1,000 births). This conclusion now is that DTG can be given to any adult as first line therapy, and that persons capable of pregnancy should be counseled about the very small risk of neural tube defects.

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**ACTIVE INGREDIENT**

Dolutegravir (50 mg)

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**INTEGRASE STRAND TRANSFER INHIBITOR**

Recommended as a component of initial regimen for most people

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Dolutegravir (50 mg)

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**ACTIVE INGREDIENT**

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**ACTIVE INGREDIENT**

Dolutegravir (50 mg)
Isentress HD (and Isentress) raltegravir RAL

Recommended as a component of initial regimen in certain clinical situations

STANDARD DOSE
ISENTRESS HD: Two 600 mg film-coated tablets once daily without regard to food 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 without regard to food 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 40 kg. Isentress is for adults and children weighing at least 4 kg (2 kg). Both Isentress HD and Isentress can be taken without regard to food. 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 participants include insomnia, nausea, and headache. The side effect profile in children is comparable to adults. See weight gain in “More information.”

Isentress may cause elevated levels of creatine phosphokinase (CPK, a muscle enzyme). Inform your provider or pharmacist if you have a history of rhabdomyolysis, myopathy, or increased creatine phosphokinase, 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 people 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. The DHHS guidelines recommend an STR. For these reasons, both the DHHS and IAS-USA guideline panels have downgraded raltegravir to “certain situations” for initial therapy. Pregnancy is one of those situations, as raltegravir appears to be safe in pregnancy, but must be given twice daily.

Background: In 2017, the original formulation, Isentress, was well tolerated and highly effective, its twice-daily dose was seen by some as a relative inconvenience. According to DHHS HIV treatment guidelines, raltegravir was recently downgraded from a preferred component of an initial regimen in most individuals to a component of a regimen in only certain clinical situations due to the higher pill burden as well as the relatively lower genetic barrier against the development of resistance compared to second generation INSTIs. Raltegravir-based regimens may be preferred for people with high cardiovascular risk. Raltegravir is a preferred drug for PEP (post-exposure prophylaxis)—preventing HIV acquisition after a potential exposure) along with dolutegravir.

Isentress is one of the preferred INSTI medications 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.

Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; go to apregistry.com.

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

AVERAGE WHOLESALE PRICE
Isentress HD 600 mg, 60 tablets: $2,185.92/month
Isentress 100 mg, 60 chewables: $546.48/month
Isentress 100 mg, 60 packets: $546.48/month
Isentress 400 mg, 60 tablets: $2,185.92/month

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 relative inconvenience. According to DHHS HIV treatment guidelines, raltegravir was recently downgraded from a preferred component of an initial regimen in most individuals to a component of a regimen in only certain clinical situations due to the higher pill burden as well as the relatively lower genetic barrier against the development of resistance compared to second generation INSTIs. Raltegravir-based regimens may be preferred for people with high cardiovascular risk. Raltegravir is a preferred drug for PEP (post-exposure prophylaxis)—preventing HIV acquisition after a potential exposure) along with dolutegravir.

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STANDARD DOSE
PREZISTA: 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. 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 flavored) available for children age 3 and older and for adults who can’t swallow pills. One 600 mg tablet with 100 mg Norvir twice daily will be accompanied by fever and/or elevations of liver enzymes, and can be life-threatening. While very rare, treatment-naïve and treatment-experienced individuals. 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. It is not recommended to co-administer Prezcobix with tenofovir disoproxil fumarate with creatinine clearance (CrCl) less than 70 mL/min.

Must also be taken in combination with another antiretroviral(s) that does not contain this medication or medication from the same drug class. Do not use either drug in people with severe liver impairment. 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
Darunavir contains a sulfra component and should be used with caution by people with known sulfonamide allergy. Most common side effects may include diarrhea, nausea, headache, rash, vomiting, and abdominal pain. 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. 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. Measure liver function before starting darunavir and then monitor, with perhaps closer monitoring for people with underlying liver problems, especially during the first several months. No dose adjustment necessary for Prezista with mild to moderate liver disease, but Prezista plus Norvir is not recommended for people with severe liver impairment. A small increase in serum creatinine (Scr) may be observed with Prezcobix that does not translate to a decrease in kidney function.

POTENTIAL DRUG INTERACTIONS
Drug interactions of Prezista plus Norvir may be different from those with Prezista plus Tybost. Tybost is not interchangeable with Norvir. Do not take with alfuzosin, dronedarone, ergot derivatives, ivabradine, methadone, nalmefene, pimozide, triazolam, oral midazolam, pimozide, triazolam, oral midazolam, cosartan, budesonide, ciclesonide, flunisolide, mometasone, triamcinolone, or voriconazole. Voriconazole should not be used unless the benefits outweigh the risks. Effectiveness of oral contraceptives may be decreased; consider using alternative methods of contraception. Increases the exposure of nasal and inhaled fluticasone and budesonide, as well as systemic corticosteroids ciclesonide, beclomethasone, dexamethasone, methylprednisolone, mometasone, rifapentine, salmeterol, ticagrelor, trimcinolone, or voriconazole. Monitor for lack of virologic response when eslicarbazepine or oxcarbazepine is needed. Initiation or dose adjustments of insulin or oral hypoglycemic medications may be required for some individuals. Apixaban dose may need to be adjusted.

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

PREZISTA AWP
600 mg, 60 tablets:
$2,338.22/month
800 mg, 30 tablets:
$2,338.22/month

PREZISTA AWP
$2,672.56/month
**STANDARD DOSE**

**REYATAZ:** 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. 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. Swallow capsules whole—do not open or mix with anything. 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). Oral powder may be used by adults who cannot swallow the capsules.

**EVOTAZ:** One tablet once daily with food in adults and pediatric patients weighing at least 77 pounds (35 kg). Each tablet contains 300 mg of atazanavir boosted by 150 mg cobicistat. Use with Integrelin or Sustiva is not recommended. Use in treatment-experienced individuals can depend on the drug-resistant virus. Not recommended for people with any degree of liver impairment or those who are treatment-experienced and on hemodialysis. Evotaz is not recommended during pregnancy due to substantially lower exposures of atazanavir and cobicistat during pregnancy.

Must be taken in combination with another antiretroviral(s) that does not contain this medication or medication from the same drug class(es). 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**

Most common side effects may include nausea, ocular icterus (yellowing of the eyes), and jaundice. The ocular icterus and jaundice are reversible upon discontinuation. Less common side effects may include kidney stones, gallstones, abdominal heart rhythm, and elevated liver enzymes (more common in people with hepatitis B or C). Atazanavir has been associated with changes to the ECG (electrocardiogram) of some people. Because of limited experience in those with preexisting heart disease, ECG monitoring should be considered in these individuals.

**REYATAZ:** Kidney laboratory testing should be performed on all individuals 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. Reyataz capsules do not contain phenylalanine but oral powder does; thus, use with caution in individuals with phenylketonuria.

**EVOTAZ:** 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. 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 people 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 people taking both cobicistat and tenofovir (DF TDF). 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 cobicistat-containing regimens.

**POTENTIAL DRUG INTERACTIONS**

Do not use with alfuzosin, rifampin, irinotecan, ergot derivatives, lovastatin, simvastatin triazolam, oral midazolam, St. John’s wort, Revatio, or Viread (nevirapine). Tenofovir is not recommended with Norvir. Proton pump inhibitors and H2-receptor antagonists can prevent atazanavir from being absorbed. Treatment-experienced people should not take PPIs while on atazanavir. See package insert for antacid dosing adjustment recommendations. If taking a chewable antacid, take with food two hours before or one hour after atazanavir dose. Treatment-experienced people should not take atazanavir with efavirenz. Tenofovir DF decreases levels of atazanavir, and Reyataz/Norvir increases tenofovir DF levels; monitor for adverse events. 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. Reyataz/Norvir as well as Evotaz increase levels of fluticasone; monitor for signs of Cushing’s syndrome. 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. Do not take with Zepatier. Can be used with Harvoni if tenofovir DF is not part of the HIV regimen. Monitor for tenofovir toxicities with Epclusa if TDF is part of the HIV regimen. Tell your provider or pharmacist about all medications, herbs, and supplements you are taking or thinking of taking, prescribed or not, as there are many other drug interactions not listed here.

**REYATAZ:** Can be taken unboosted with Eviplera if absolutely necessary (Reyataz dose of 400 mg daily). Bepridil, amiodarone, quinidine, and lidocaine should be taken with caution. Use caution when taking Itraconazole or ketoconazole. Voricosta is not recommended. Reyataz can be taken with birth control pills that contain no more than 30 mcg of ethinyl estradiol if taking Reyataz without ritonavir, and at least 35 mcg if taken with it. Use caution with carbachol, phenobarbital, and phenytoin. Take lower dose of colchicine. Use with ritonavir when taking buprenorphine; monitor for sedation.

**EVOTAZ:** Do not take with lurasidone, pimozide, ranolazine, or dronedarone. 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.

**MORE INFORMATION**

Yellowing of the eyes is a common reason for discontinuation.

**MANUFACTURERS**

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

**REYATAZ AWP**
Not available on formulary used

**GENERIC ATAZANAVIR AWP**
150 mg, 60 capsules: $1,517.10/month
300 mg, 30 capsules: $1,502.76/month

**REYATAZ AWP**
$1,926.56/month
Norvir is a pharmacokinetic enhancer (booster) and an antiretroviral protease inhibitor. It is used as a booster for other drugs, recommended as a component of initial regimen in certain clinical situations. Norvir RTV is a protease inhibitor used with another protease inhibitor to increase the blood levels of the other protease inhibitor. Norvir is available in pink and orange tablets in 200 mg and 400 mg strengths.

**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.

**POTENTIAL SIDE EFFECTS AND TOXICITY**

The side effect potential of Norvir and other protease inhibitors (the class of drugs to which Norvir belongs) includes 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 impairment, 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, rivaroxaban, 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. Certain medications are metabolized by CYP3A4 and CYP2C19 enzymes, and inhibitors of these enzymes 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). If you are pregnant, 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.

**DR. MELANIE THOMPSON:**

Ritonavir is now used only as a booster to raise the levels of other drugs, usually other protease inhibitors. Its main downside is the long list of drug interactions it causes, some of them dangerous. If you take ritonavir, always consult your HIV care provider before taking OTC drugs, and always inform anyone who is prescribing drugs for you that you are taking ritonavir. Sadly, not all care providers are familiar with its drug interactions. Norvir tablets or capsules; on the other hand, are awesome at this. You can look up drug interactions at hiv-druginteractions.org.

The most common side effects are gastrointestinal, including diarrhea, nausea, and vomiting. Somewhat unusual but common side effects include tingling of the mouth and taste disturbance. These are all less at lower doses that are used for boosting.

The breaking news about ritonavir is that it is now packaged as a component of Paxlovid, a new oral COVID treatment (see page 17). People already taking ritonavir or cobicistat can add Paxlovid to the mix (only 5 days of treatment) as it should not cause additional drug interactions. It could cause some additional side effects, so this should be discussed with an HIV care provider, if possible; if you are prescribed Paxlovid by someone other than your HIV care provider, be sure they are aware of all the medicines you take. HIVMA and IDSA have made some recommendations; here: idsociety.org/globalassets/ covid-19-real-time-learning-network/patient-populations/hiv-oral-covid-tx-considerations-for-people-with-hiv-and-hcv.pdf. The NIH COVID-19 and treatment guidelines panel has a statement on Paxlovid here: covid19treatmentguidelines.nih.gov/therapies/statement-on-paxlovid-drug-drug-interactions/.

**ACTIVIST MICHAEL BRODER:**

At therapeutic doses, Norvir may cause considerable nausea, vomiting, and diarrhea, so it was not an ideal choice for treatment. Boosting of PIs with low-dose ritonavir became standard. A downside of boosting is that it may increase side effects of the boosted PI. And Norvir, even at low doses, may still cause GI side effects. Given newer options, there is little need for a boosted PI these days. If your provider recommends a Norvir-containing regimen, they may have a good reason, but make sure they tell you why it is.

**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.

**MANUFACTURER**

AbbVie

norvir.com; (800) 633-9110

**AVERAGE WHOLESALE PRICE**

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

positivelyaware.com/norvir | MARCH+APRIL 2022 37
Tybost interacts with many drugs.

**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 Prezocibix), 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; anyone taking darunavir 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 people) 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. While cobicistat does not affect actual kidney function, its effect on SCr can make monitoring of impaired kidney function more difficult or less accurate.

**POTENTIAL DRUG INTERACTIONS**

Tybost interacts with many drugs. Of note, Tybost is not interchangeable with Norvir. Do not take with alfuzosin, colchicine, dicyclomine, disopyramide, dronedarone, ergotamine, irinotecan, simvastatin, lovastatin, lurasidone, methylgeronovine, 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, anti-depressants, 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 OxyContin, Vlekira 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 methamphetamine. Tell your provider or pharmacist about all medications, herbs, 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 drug levels of atazanavir and once-daily darunavir, and is part of the STRs containing elvitegravir. However, you cannot just substitute COBI for ritonavir in all circumstances. For example, it should not be used twice daily with darunavir 600 mg.

COBI has no antiviral effect, but it does have all of the drug interactions of ritonavir and some that are different. There are quite a few drugs that absolutely can’t be taken with cobicistat. Rather than trying to memorize these or other drug interactions, look them up at hvdruginteractions.org and discuss with an HIV care provider. Many of these can be managed by dose changes, but not always. Be sure that anyone prescribing drugs for you knows that you take a cobicistat-containing regimen.

COBI will raise your blood creatinine level, but only by about 0.4 mg/dL or less. This is due to changes in secretion by the kidneys and not because of kidney disease. However, when COBI is used with TDF, some serious kidney side effects may be seen, so kidney function should be watched closely.

Cobicistat-containing regimens should not be taken in pregnancy due to inadequate drug levels of COBI and the drug it boosts in the second and third trimester. However, if you are pregnant and already on a COBI-containing regimen discuss with your HIV care provider whether it is safe to continue.

**NEW COVID treatment**

The new COVID treatment Paxlovid includes ritonavir, but it can be taken in addition to a cobicistat-containing regimen, with attention to possible side effects. (See “Norvir.”)

**DR. MELANIE THOMPSON:**

Cobicistat is used to boost drug levels of atazanavir and once-daily darunavir, and is part of the STRs containing elvitegravir. However, you cannot just substitute COBI for ritonavir in all circumstances. For example, it should not be used twice daily with darunavir 600 mg.

COBI has no antiviral effect, but it does have all of the drug interactions of ritonavir and some that are different. There are quite a few drugs that absolutely can’t be taken with cobicistat. Rather than trying to memorize these or other drug interactions, look them up at hivdruginteractions.org and discuss with an HIV care provider. Many of these can be managed by dose changes, but not always. Be sure that anyone prescribing drugs for you knows that you take a cobicistat-containing regimen.

COBI will raise your blood creatinine level, but only by about 0.4 mg/dL or less. This is due to changes in secretion by the kidneys and not because of kidney disease. However, when COBI is used with TDF, some serious kidney side effects may be seen, so kidney function should be watched closely.

Cobicistat-containing regimens should not be taken in pregnancy due to inadequate drug levels of COBI and the drug it boosts in the second and third trimester. However, if you are pregnant and already on a COBI-containing regimen discuss with your HIV care provider whether it is safe to continue.

**ACTIVEVIST MICHAEL BRODER:**

Tybost (cobicistat, approved 2014) is a pharmacokinetic booster. By inhibiting a certain enzyme pathway in the liver, Tybost boosts levels of other drugs, including PI and INSTI. Tybost is used to boost the PIs atazanavir (Reyataz + Tybost = Evotaz) and darunavir (Prezista + Tybost = Prezcobix). Tybost is also used to boost the INSTIs elvitegravir (in Genvoya and Stribild). A downside of boosting is that it may increase side effects of the boosted drug (PI or INSTI). Given newer options, there is little need for a boosted PI or INSTI these days. If your provider recommends a Tybost-containing regimen, they may have a good reason, but make sure they tell you what it is.

**MANUFACTURER**

Gilead Sciences, Inc.

gilead.com; tybost.com

(800) GILEAD-5 (445–3235)

**AVERAGE WHOLESALE PRICE**

$321.02/month
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 people 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. Data associate INSTIs and TAF with potential weight gain. 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. New TAF information as of last year: “Post-marketing cases of renal (kidney) impairment, including acute renal failure, proximal renal tubulopathy (PRT), and Fanconi syndrome have been reported with TAF-containing products; while most of these cases were characterized by potential confounders that may have contributed to the reported renal events, it is also possible these factors may have predisposed people to tenofovir-related adverse events.” At initiation and during treatment, assess kidney lab tests: serum creatinine, estimated creatinine clearance, urine glucose, and urine protein. In people with chronic kidney disease, also assess serum phosphorus. Discontinue Descovy in people who develop clinically significant decreases in kidney function or signs of Fanconi syndrome.

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 HBV who have discontinued Descovy (due to elimination of both emtricitabine and TAF, which also treat hepatitis B). Monitor liver enzymes closely in people co-infected with HBV 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 Temixos, 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 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 Elclusa, Harvoni, or Zepatier. Tell your provider or pharmacist about all medications, herbs, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions that are not listed here.

MORE INFORMATION

Descovy is similar to Truvada, except that instead of TDF (tenofovir disoproxil fumarate), Descovy contains TAF (tenofovir alafenamide), which reduces serum tenofovir concentration by 90%. This results in a decreased impact on kidney and bone demineralization but maintains potent antiretroviral 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 people 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—in fact, one or the other combination is found in some of the single-tablet regimens. Descovy can be used for HIV prevention; 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 HBV. Pediatric HIV guidelines recommend Descovy as part of a preferred regimen. TAF is an alternative NRTI in the Antiretroviral Pregnancy Registry through their provider, go to apregistry.com.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$2,446.60/month

DR. MELANIE THOMPSON:

Descovy is Truvada with the newer version of tenofovir, TAF, substituted for TDF. Along with Truvada, it is recommended for initial therapy for most people in combo with an INSTI anchor drug. TAF/FTC is also included in Symtuza and Odensey. Clinical trials found TAF to be associated with lower rates of biomarkers for kidney impairment and bone density loss than TDF, owing to higher intracellular and lower blood levels of tenofovir. Much is made of Descovy being “safer” than Truvada, but, in my opinion, these changes are often not clinically significant for young, healthy people without comorbidities, and for anyone not taking booster drugs. LDL and HDL cholesterol and weight gain are higher with Descovy than Truvada. Like Truvada, Descovy is active against hepatitis B, owing to the activity of both TAF and FTC.

Because of reassuring data from the Antiretroviral Pregnancy Registry, TAF is now recommended as an alternative drug in pregnancy by the DHHS Perinatal Guidelines panel.

ACTIVIST MICHAEL BRODER:

I am on a Descovy-containing regimen. TAF may be safer than TDF for bones and kidneys. This is especially important for people under age 25, who are still actively developing bone, and for people who have mild to moderate kidney disease. On the other hand, TAF has a worse profile than TDF when it comes to cholesterol and weight gain. Providers will weigh the choice based on their experience, and on the needs of each patient.

positivelyaware.com/descovy | MARCH+APRIL 2022 39
**STANDARD DOSE**
One tablet once daily without regard to food for adults and children weighing at least 77 pounds (35 kg). Tablet contains 200 mg emtricitabine and 300 mg tenofovir disoproxil fumarate. 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) doses: 100/150 mg tablets, 133/200 mg tablets, 167/250 mg tablets, and 200/300 mg tablets. Tablets may be dissolved 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 HBV who have discontinued Truvada (due to either death or loss of benefit from both emtricitabine and TDF, which also treat hepatitis B). Monitor liver enzymes closely in people co-infected with HBV 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 people sensitive to lactose.

**POTENTIAL DRUG INTERACTIONS**
Do not take with Cimduo or Temixys, Descovy, Emtriva, Epivir-HBV, Hespera, 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 for HIV treatment, 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 Hepaterv, depending on the third drug in the HIV regimen; monitor for tenofovir toxicities if used with Eplucsa. Tell your provider or pharmacist about all medications, herbas, and supplements you are taking or thinking of taking, prescribed or not, as there are 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. 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 people 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 of HIV treatment in pregnancy. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; go to aregistry.com.

**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

**DR. MELANIE THOMPSON:**
Tenofovir disoproxil fumarate (TDF) rose to predominance as a backbone because of lower toxicity than AZT and the “d-drugs” (d4T, ddi, ddC) and its high genetic barrier to resistance. It also has potent activity against hepatitis B. Today it is almost always given with FTC or 3TC as in Truvada, Cimduo, and Temixys.

While diarrhea, nausea, and fatigue were the most common side effects seen in early clinical trials, people who have used TDF to modify their virus have reported a potential for kidney toxicity, mostly mild but occasionally serious, and decrease in bone density. Serious toxicities are most often seen in people with other risks for kidney or bone disease, including older age or comorbidities, or when taken in combination with ritonavir or cobicistat. TDF also lowers LDL and HDL cholesterol and is associated with a bit of weight loss. TDF/FTC is safe in pregnancy.

**ACTIVIST MICHAEL BRODER:**
Approved in 2004, Truvada is a fixed-dose combination (FDC) of two NRTIs (emtricitabine and tenofovir disoproxil fumarate, TDF). Truvada is recommended in combination with Tivicay for most people starting therapy for the first time. The components of Truvada are included in the single-tablet regimens Atripla, Stridifb, and Complera. Truvada has largely been supplanted by Descovy, which replaces the TDF in Truvada with tenofovir alafenamide (TAF). TAF may be safer than TDF for bones and kidneys. This is especially important for people under 25, who are still actively developing bone, and for people who have a history of moderate to severe kidney disease. On the other hand, TDF may be better than TAF when it comes to cholesterol and weight gain. If your provider recommends Truvada rather than Descovy, they may well have a good reason, but make sure they tell you what it is.
Cimduo and Temixys

Fixed-dose combinations of two nucleoside reverse transcriptase inhibitors (nucleosides, or “nukes”)

Recommended as components 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 urinary 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 HBV who have discontinued medication (due to elimination of both lamivudine and TDF, which also treat hepatitis B). Monitor liver enzymes closely in people co-infected with HBV and, if appropriate, initiation of anti-hepatitis B therapy may be made by 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 people sensitive to lactose. Read weight discussion in this online version of this page.

**POTENTIAL DRUG INTERACTIONS**
Do not take with Descovy, Entriva, Epivir-HBV, Hepsera, Truvada, Vemidyl, 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 Encluba. Tell your provider or pharmacist about all medications, herbs, 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 formulations (such as with Delstrigo, Symfi, and Synri, Lo). 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 people 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. Cimduo and Temixys are recommended by DHHS as one of the preferred NRTI combination components of an ART regimen during pregnancy. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

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

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

**AVERAGE WHOLESALE PRICE**
Cimduo: $1,208.56/month
Temixys: Not available on formulary used

**DR. MELANIE THOMPSON:**
Tenofovir disoproxil fumarate (TDF) rose to prominence as a backbone because of lower toxicity than AZT and the “d-drugs” (d4T, ddI, ddC) and its high genetic barrier to resistance. It also has potent activity against hepatitis B. Today it is almost always given with FTC or 3TC as in Truvada, Cimduo, and Temixys. Generic TDF now is combined with generic 3TC in Cimduo and Temixys, essentially the same “brand” drugs, they are called “generic” manufacturers. Technically as combination drugs, they are “brand” drugs. This gets me on my soapbox about egregious pricing for drugs. Copay cards allow companies to maintain very high drug prices while making them affordable enough for people to actually take them. So, while these prices are less than that of Truvada, they pack in an outsized profit for the maker. TDF/3TC combinations are not approved for PrEP.

**ACTIVIST MICHAEL BRODER:**
Cimduo and Temixys were both approved in 2018 and are fixed-dose combinations (FDCs) of two NRTIs. They come from different manufacturers: Cimduo from Mylan Pharmaceuticals and Temixys from Celltrion. This combination was not possible when these drugs were under patent, because they were made by competing drug companies. After both drugs went off patent, generic drug companies could mix and match. Cimduo and Temixys are basically branded generic versions of Truvada, as the emtricitabine in Truvada is closely chemically related to lamivudine (you did not hear me say “identical”) and is more-or-less equivalent products, a little like Coke and Pepsi, or Nike and Reebok. Gilead’s patent on emtricitabine will soon fall, and there are already over a dozen FDA approved generics available. As HIV drugs start to go generic, trust your provider to know what’s what—just verify.
**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) that do 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, alternate doses can be obtained by using the individual components of this medication as needed.

**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 Zidovudine 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 an HSR, but the risk is reduced to 1% or less from clinical studies. This test is covered by most insurance and also by LabCorp/ViIV (see company contact on co-pay chart). A warning card should be included with this medication when dispensed from the pharmacy. Some 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, 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 with cardiac risk, although theoretical contributing mechanisms have been described. 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 HBV who have discontinued Epzicom (due to elimination of the lamivudine component, which also treats HBV). Monitor liver enzymes closely in people co-infected with HBV 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; pain or fullness; loss of appetite; pain, achiness, or tenderness on the right side below the ribs.

**POTENTIAL DRUG INTERACTIONS**

See the individual drugs contained in Epzicom—Epivir and Ziajen. 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: Atiprida, Biktarvy, Combivir, Completra, Deisolgi, Descovy, Dovato, Emtriva, Epivir, Genvoya, Odefsey, Stribild, Symfi (including Symfi Lo, Symtuza, Temixys, Triumeq, Trizivir, Truvada, or Ziajen); also, Epivir-HBV is used for the treatment of hepatitis B. Alcohol can increase 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, herbs, 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 HIV treatment in pregnancy. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider, go to aregistry.com.

**MANUFACTURER**

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

**AVERAGE WHOLESALE PRICE**

$1,550.05/month

generic: $1,395.05/month
Emtriva

**Nucleoside reverse transcriptase inhibitor (nucleoside, or “nuke”)**

Recommended as a component of initial regimen for most people

### STANDARD DOSE

One 200 mg capsule once daily without regard to food for adults and children regardless of age. 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). Emtriva is dosed based on body weight for children. See the package insert for weight-based dosing. Emtriva is also available as an oral solution (10 mg/mL) for children aged 0–3 months (3 mg/kg), children aged 3 months to 17 years (6 mg/kg), and adults (10 mg/kg) who are not able to swallow the capsules. Liquid dose is up to a maximum of 240 mg (24 mL) daily; the 200 mg capsule equals 240 mg solution. Emtriva oral solution should be kept in the refrigerator. If kept at room temperature, the oral solution should be used within three months. Emtriva can be substituted for Epivir.

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

### POTENTIAL SIDE EFFECTS AND TOXICITY

Emtriva is very well tolerated. The most common side effects (which were 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 HBV who have discontinued Emtriva (because emtricitabine also treats hepatitis B). Monitor liver enzymes closely in people co-infected with HBV and, if appropriate, initiation of anti-hepatitis B therapy may be warranted upon discontinuation of Emtriva. 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, which are used for treatment of hepatitis B. No other significant drug interactions are predicted. Emtriva may be used with hepatitis C drugs such as Eclusa, Harvoni, or Zepater, depending on the other components in the HIV regimen. Tell your provider or pharmacist about all medications, herbs, and supplements you are taking or thinking of taking, prescribed or not.

### MORE INFORMATION

This drug is used as a component 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 contain Emtriva, and 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, Stridil, 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 Truvada (tenofovir), and for that reason, some providers continue Emtriva treatment in combination with other antiretrovirals after resistance develops. The capsule is small, which is an advantage for people with difficulty swallowing. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO aregistry.com.

### MANUFACTURER

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

### AVERAGE WHOLESALE PRICE

<table>
<thead>
<tr>
<th><strong>emtriva</strong></th>
<th><strong>$643.82/month</strong></th>
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<tbody>
<tr>
<td>generic FTC</td>
<td><strong>$579.37/month</strong></td>
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### DR. MELANIE THOMPSON:

Emtricitabine, also called FTC, is generally coformulated with TDF or TAF as a dual nuke regimen, and as part of many STRs. It has the same resistance profile as FTC and is regarded as interchangeable with TDF by guidelines panels. An unusual side effect, hyperpigmentation of palms and soles, was noted in some early clinical trials, yet we never hear about this one any more.

There is no food requirement with FTC, but dosage requires adjustment according to kidney function.

### ACTIVIST MICHAEL BRODER:

Emtriva (emtricitabine, approved in 2003) is an NRTI. It is included in the fixed-dose combinations (FDCs) Truvada and Descovy, and in the single-tablet regimens (STRs) Atripla, Biktarvy, Complera, Genvoya, Odefsey, Stridil, and Symtuza, and in its generic form in the STRs Symfi and Symfi Lo. Emtriva is among the safest, most tolerable, and most convenient HIV drugs available. The only side effect that was more common among people taking Emtriva than other HIV drugs in clinical trials was skin discoloration on the palms or soles of the feet. This side effect, occurring mostly in non-White people, was mild and did not result in treatment discontinuation. Its mechanism and clinical significance remain unknown. Emtriva is a close chemical relative of Epivir (lamivudine). In 2003, Gilead Sciences purchased Triangle Pharmaceuticals with the express intention of combining Triangle’s Emtriva with Gilead’s Viread to make Truvada, which proved to be a very savvy business move.
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. 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 or symptoms of hepatitis B therapy may be warranted.

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. Epivir 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 (which were rarely reported) 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 HBV 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 B: 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, achiness, or tenderness on the right side below the ribs.

POSSIBLE DRUG INTERACTIONS
Do not take with Cimduo or Temixys, Descovy, Emtriva, Epivir-HBV, Hespera, or Truvada, which are used for the treatment of hepatitis B. No other significant drug interactions are known. It 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, herbal 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 HBV 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 Vemid (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). Epzicom is recommended as a preferred initial regimen in pregnancy. Epivir as part of the combination tablet Combivir is recommended as an alternative NRTI combination regimen of an HIV treatment 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 people 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 people who can’t physically tolerate generic regimens. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider.

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

AVERAGE WHOLESALE PRICE
Epivir Not available on formulary used
generic lamivudine 150 mg, 60 tablets: $429.66/month
generic lamivudine 300 mg, 30 tablets: $429.66/month

POTENTIAL DRUG INTERACTIONS
Nucleoside reverse transcriptase inhibitor (nucleoside, or “nuker”)

Recommended as a component of initial regimen for most people

DR. MELANIE THOMPSON:
Lamivudine or 3TC is the oldest HIV med still in widespread use, generally paired with abacavir or TDF. It is viewed by guidelines panels as interchangeable with FTC for treatment, but not intended for prevention. It is included in Triumeq, Delstrigo, Dovato, Symfi, Symfi Lo, Cimduo, and Temixys, as well as the dual nuke combos Epzicom and Combivir. Resistance occurs rapidly when virus breaks through, but its signature resistance mutation, M184V, has a beneficial effect on some other drugs like AZT and tenofovir. It also has some activity against hepatitis B.

ACTIVIST MICHAEL BRODER:
Approved in 1995, Epivir (lamivudine) was one of the first five NRTIs, and the only one still in wide use. Epivir is among the safest, most tolerable, and most convenient HIV drugs available, with no significant side effects. A very potent drug, it is half of a complete HIV regimen when combined with the INSTI dolutegravir, co-formulated as the single-tablet regimen (STR) Dovato. Epivir is also part of a complete HIV regimen when combined with Tivicay (dolutegravir) and tenofovir alafenamide (TAF) or tenofovir disoproxil fumarate (TDF). The generic form, lamivudine, is included in the branded generic fixed-dose combinations (FDs) Cimduo and Temixys (alongside TDF). Epivir is a close chemical relative of Emtriva (emtricitabine); but for what it’s worth, Epivir came first, and Emtriva was brought to market specifically to compete with Epivir—which it has done quite successfully for some 20 years.
**Viread**
tenofovir disoproxil fumarate

**TDF**
Nucleoside reverse transcriptase inhibitor (nucleoside, or “nuke”)

**Recommends as component of initial regimen for most people**

**STANDARD DOSE**
One 300 mg tablet once daily, without regard to food. Must be taken in combination with other antiretrovirals.

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 dissolved in water, grape juice, or orange juice with minor stirring and pressure from a spoon. In children, Viread dose is based on body weight. See package insert for specific 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. 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 people 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. Decreased bone density (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. While calcium and vitamin D levels monitoring should be considered for these supplements, talk with your provider before starting on these 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 change in urinary habits, as these could be bone and kidneys, which makes the two drugs into the blockbuster fixed-dose combination (FDC) Truvada. Viread is potent, tolerable, convenient, and has a good resistance profile. Its downside is its negative impact on bone and kidneys, which makes it safer alternatives to Viread.

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 HBV and HIV who have discontinued Viread (because TDF also treats hepatitis B). Monitor liver enzymes closely in people co-infected with HBV and, if appropriate, initiation of anti-hepatitis B therapy may be warranted upon discontinuation of Viread. 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; loss or teardrop-like, bone, or muscle pain; loss of appetite; itchiness or vomiting; loss of appetite; fever, aching, or tenderness on the right side below the ribs. Viread's formulation contains lactose, which can cause some abdominal discomfort, especially in people sensitive to lactose.

**POTENTIAL DRUG INTERACTIONS**
Do not take with Cimduo or Temixys, Descovy, Hepsera, Truvada, or Vemilidy, 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. People 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, herbal, 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 NRTI combinations recommended 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. 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 Stridbl. Truvada, Cimduo, and Temixys are recommended by DHHS as part of the preferred NRTI combination components of an ART regimen during pregnancy. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; go to apregistry.com.

**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

**DR. MELANIE THOMPSON:**
The “original” tenofovir, tenofovir disoproxil fumarate (TDF) is used for both HIV and hepatitis B treatment (at different doses) and is generally given with FTC or FTC. Its most worrisome side effects are kidney toxicity and loss of bone density, especially when used with a ritonavir or cobicistat booster, or when used by persons with other risk factors for kidney disease or bone loss. For further information, see Truvada.

**ACTIVIST MICHAEL BRODER:**
Viread (tenofovir disoproxil fumarate, TDF; approved in 2001) is an NRTI, and was the first HIV drug brought to market by Gilead Sciences, the market leader in drugs to treat and prevent HIV (in a decades-long rivalry with ViV HealthCare). In 2003, Gilead acquired Triangle Pharmaceuticals, along with its newly approved NRTI, emtricitabine (Emtriva), and combined the two drugs into the blockbuster fixed-dose combination (FDC) Truvada. Viread is potent, tolerable, convenient, and has a good resistance profile. Its downside is its negative impact on bones and kidneys, which makes its safety questionable, especially for people under age 25, who are still actively developing bone, and for people who have even mild to moderate kidney disease. Nowadays, there are a number of safer alternatives to Viread. If your provider recommends a Viread-containing regimen, they may well have a good reason, but make sure they tell you what it is.
**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 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 diarrhea. 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 an 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 aches, chills, diarrhea, vomiting, abdominal pain, respiratory symptoms (cough, difficulty breathing, or wheezing), and cardiac 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 nausea and vomiting, and you can never take abacavir or any product containing abacavir (Epzicom, Ziagen, or Triumeq) again (starting again is called rechallenge), 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 six 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, family history of heart disease, and drug use), especially within the first six 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, although theoretical contributing mechanisms have been described.

**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 within their preferred viral load was over 100,000 copies/mL. However, when combined with Tivicay (dolutegravir), Epzicom performed just as well as Truvada in people with high viral loads over 100,000 copies/mL (Hence, Triumeq is the only abacavir-containing regimen recommended by DHHS as initial therapy for most HLA-B*5701-negative people. It is recommended that people with symptoms of acute respiratory disease consider HSR even if another diagnosis such as pneumonia, bronchitis, or flu is possible. But again, a simple test reveals whether you are at high risk for the allergic reaction. FDA researchers reported finding a mechanism for autoimmune drug reactions, including abacavir HSR, and hope it helps improve drug safety in the future. Ziagen as part of the combination tablet Epzicom is recommended by DHHS as one of the preferred NRTI combination components of an ART regimen during pregnancy, and as a preferred backbone drug in combination with lamivudine (Epivir) or emtricitabine (Emtriva) for pediatric use in ages one month and older. With abacavir recommended as a preferred drug for pediatrics, DHHS moved zidovudine from the “Preferred” list to the “Alternate” list last year for this population. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

**RECOMMENDED AS A COMPONENT OF INITIAL REGIMEN for most people when used in combination with dolutegravir and lamivudine (as Triumeq)**

**MANUFACTURER**

ViiV Healthcare
viiivhealthcare.com
(877) 844-8872

**AVERAGE WHOLESALE PRICE**

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

People who are at high risk for heart disease should discuss risks with their provider and they should be monitored more closely.

**DR. MELANIE THOMPSON:**

One of the older drugs still in use, abacavir is generally paired with 3TC as a nuke backbone (Epzicom) and is part of the STR Triumeq. Before starting abacavir, a blood test for HLA-B*5701, a genetic marker, should be done to identify people who should not take the drug because of high risk for a potentially life-threatening hypersensitivity reaction. Since using this test, abacavir hypersensitivity is uncommonly seen. If you have an HSR, but the risk is very low (1% from clinical studies). However, abacavir was associated with increased risk for cardiovascular disease in some, but not all, large observational studies. The FDA considers the risk to be “inconclusive,” but the DHHS guidelines recommend avoiding abacavir in persons with, or at high risk for, cardiovascular disease.

**ACTIVIST MICHAEL BRODER:**

Ziagen (abacavir, approved in 1998) is one of the older drugs still in use, abacavir is generally paired with 3TC as a nuke backbone (Epzicom) and is part of the STR Triumeq. Before starting abacavir, a blood test for HLA-B*5701, a genetic marker, should be done to identify people who should not take the drug because of high risk for a potentially life-threatening hypersensitivity reaction. Since using this test, abacavir hypersensitivity is uncommonly seen. If you have an HSR, but the risk is very low (1% from clinical studies). However, abacavir was associated with increased risk for cardiovascular disease in some, but not all, large observational studies. The FDA considers the risk to be “inconclusive,” but the DHHS guidelines recommend avoiding abacavir in persons with, or at high risk for, cardiovascular disease. Even though Ziagen is a component of an ART regimen that is recommended by current guidelines, there are a number of other options that are just as effective, tolerable, and convenient, and may be safer. If your provider recommends a Ziagen-containing regimen, they may well have a good reason, but make sure they tell you what it is.

**DR. MELANIE THOMPSON:**

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**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) with viral load less than or equal to 100,000. 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 people 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/mm³ before starting Edurant due to higher rates of virologic failures (19.4%—seven out of 36 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. Edurant also has minimal negative effects on LDL (“bad”) cholesterol, total cholesterol, and triglycerides compared to Sustiva. Edurant improved an increase in 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 people without a history of liver disease. Edurant improved an increase in kidney function test (serum creatinine) within the first four weeks of treatment. The changes are not considered clinically relevant.

**POSSIBLE 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. Edurant also has minimal negative effects on LDL (“bad”) cholesterol, total cholesterol, and triglycerides compared to Sustiva. Edurant improved an increase in 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 people without a history of liver disease. Edurant improved an increase in kidney function test (serum creatinine) within the first four weeks of treatment. The changes are not considered clinically relevant.

**POTENTIAL DRUG INTERACTIONS**

Edurant cannot be taken with the antiretroviral medications abacavir, lamivudine, or stavudine, or with ritonavir, efavirenz, rifampin, or rifapentine; the antiviral medications clarithromycin, amoxicillin, or clarithromycin; or the antifungal medications azole, voriconazole, and fluconazole; the antidepressant medications fluoxetine, sertraline, paroxetine, and venlafaxine; or the anticonvulsant medications phenytoin, phenobarbital, or carbamazepine. The antihistamine medication cetirizine; the cannabinoid medication nabilone; the antipsychotic medication haloperidol; the antidepressant medication amitriptyline; and the antiarrhythmic medication tocainide can also affect drug absorption and may lead to resistance.

**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 in 2021 along with a long-acting injectable formulation of cabotegravir to form a complete regimen given once a month or once every two months; see Cabenuva. Edurant is not DHHS recommend for treatment-naïve people with a pre-treatment viral load greater than 100,000 copies/mL and CD4 T cell count below 200 cells/mm³. 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 lower 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 people 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 backbone 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. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

**MANUFACTURER**

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

**AVERAGE WHOLESALE PRICE**

$1,543.10/month

**ACTIVIST MICHAEL BRODER:** Edurant (rilpivirine, approved in 2011) is an NNRTI that is recommended in certain clinical situations in combination with Truvada or Descovy (or their components, tenofovir and emtricitabine), but not for people with viral load greater than 100,000 copies/mL due to higher rates of virologic failure in that group. Edurant is included in the single-tablet regimens (STRs) Complera, Juluca, and Odefsey. Edurant is one pill once a day that may or may not have been related on another regimen for at least six months. For people with no other available options, Edurant is not an obvious first choice for most people. If your provider recommends Edurant, they may have a good reason, but make sure they tell you what it is.
Pifeltro

doravirine

DOR

Non-nucleoside reverse transcriptase inhibitor
(non-nucleoside, or “non-nuke”)

Recommended as a component of initial regimen
in certain clinical situations (as a component of 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 people with severe liver impairment.

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

POSSIBLE 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 (3%). These are a common side effect of the NNRTI class, 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 NNRTIs. Doravirine did not appear to negatively affect cholesterol in studied populations.

POSSIBLE DRUG INTERACTIONS

When taken with 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, phenytoin, and phenobarbital; the androgen receptor inhibitor enzalutamide; the antimycobacterials rifampin and rifabutin; the cytotoxic agent (cancer drug) mitotane; and the herbal St. John’s wort. Tell your provider or pharmacist about all medications, herbs, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions that are not listed here.

MORE INFORMATION

FDA approved in 2018, Doravirine may be an option for people 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 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 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. Moreover, the emergence of resistance at the time of virologic failure has been reported with doravirine. Doravirine tolerability advantages over efavirenz and ritonavir-boosted darunavir. Also, doravirine has the androgen receptor blocker enzalutamide. There are other drugs that have manageable interactions, so talk with your HIV care provider about any other drugs you take.

Dr. Melanie Thompson:
Doravirine is the newest NNRTI and was never tested head-to-head against INSTIs, thus relegating it to a secondary place in DHHS and IAS-USA guidelines. Its STR version is Delstrigo. Compared with efavirenz, doravirine was associated with less nausea and rash as well as fewer neuropsychiatric side effects such as dizziness, abnormal dreams, and sleepiness, and it caused less diarrhea compared with ritonavir-boosted darunavir. LDL, triglycerides, and total cholesterol went up with efavirenz and ritonavir-boosted darunavir but down with doravirine. In a cross-study analysis, average weight increase was more with doravirine (1.7 kg) than with efavirenz (0.6 kg) and about the same as with ritonavir-boosted darunavir (1.4 kg) at week 48 but all were similar at week 96. Some drugs can’t be taken with doravirine, including some seizure and tuberculosis medications, St. John’s wort, and the androgen receptor blocker enzalutamide. There are other drugs that have manageable interactions, so talk with your HIV care provider about any other drugs you take.

ACTIVIST MICHAEL BRODER:
Pifeltro (doravirine, approved in 2018) is an NNRTI recommended in certain clinical situations as part of the single-tablet regimen (STR) Delstrigo, or in combination with either formulation of tenofovir plus either lamivudine or emtricitabine (for example, Descovy, Truvada, Cimduo, or Temixys). Pifeltro is approved both for initial therapy and for “stable switches” (use by folks undetectable on another regimen for at least six months). Unlike the NNRTI Edurant (rilpivirine), Pifeltro can be used regardless of viral load, can be taken without food, and does not interact with proton pump inhibitors (a kind of antacid). Pifeltro does, however, interact with some less commonly used drugs (ask your provider). Safety of Pifeltro in pregnancy has not yet been determined. Given other available options, Pifeltro is not an obvious first choice for most people nowadays. If your provider recommends Pifeltro, they may have a good reason, but make sure they tell you what it is.

Dr. Melanie Thompson:

Doravirine is the newest NNRTI and was never tested head-to-head against INSTIs, thus relegating it to a secondary place in DHHS and IAS-USA guidelines. Its STR version is Delstrigo. Compared with efavirenz, doravirine was associated with less nausea and rash as well as fewer neuropsychiatric side effects such as dizziness, abnormal dreams, and sleepiness, and it caused less diarrhea compared with ritonavir-boosted darunavir. LDL, triglycerides, and total cholesterol went up with efavirenz and ritonavir-boosted darunavir but down with doravirine. In a cross-study analysis, average weight increase was more with doravirine (1.7 kg) than with efavirenz (0.6 kg) and about the same as with ritonavir-boosted darunavir (1.4 kg) at week 48 but all were similar at week 96. Some drugs can’t be taken with doravirine, including some seizure and tuberculosis medications, St. John’s wort, and the androgen receptor blocker enzalutamide. There are other drugs that have manageable interactions, so talk with your HIV care provider about any other drugs you take.

There are not enough data to recommend doravirine in pregnancy.

Manufacturer:
Merck and Co.
pifeltro.com
(800) 672–6372
AVERAGE WHOLESALE PRICE
$1,916.64/month

For more information, visit the manufacturer’s website.
Sustiva efavirenz

Non-nucleoside reverse transcriptase inhibitor (non-nucleoside, or “non-nuke”)

战士职业 IS AVAILABLE

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 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.

POSSIBLE 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 people 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 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 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. Individuals in their first trimester of pregnancy are recommended to continue taking efavirenz, but for treatment-naïve 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.

POSSIBLE 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 people taking 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 as oral solution with food when taken with Sustiva. 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 people with baseline HIV viral load over 100,000 copies/mL due to increased risk for virologic failure in this group. When taken with carbamazepine, phe- nobarbital, or phenytoin, periodic monitoring of anticonvulsant use may be recommended. 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 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, herbs, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions that are not listed here.

MORE INFORMATION
If you can’t sleep, ask your doctor about gradually adjusting the timing of your dose until it’s taken during the day. A rare genetic trait affecting drug metabolism of Sustiva, leading to a higher rate of side effects, occurs more often 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 West African countries, an NNRTI would not be recommended as HIV-2 is inherently resistant to NNRTIs. Efavirenz is found in the single-tablet regimens

Dr. Melanie Thompson: Efavirenz-based regimens are no longer recommended for initial therapy due to multiple side effects, many of them affecting the central nervous system (see Atripla, Symfi and Symfi Lo). It also raises cholesterol and triglycerides, and has substantial drug-drug interactions that must be managed. Also, efavirenz should be taken on an empty stomach for best absorption. When used, it should only be given with TDF or TAF + FTC or 3TC. There is little rationale for prescribing efavirenz-based regimens at this time, although it is still recommended during pregnancy.

Activist Michael Broder: Sustiva breathed new life into the NNRTI class when it was on life support in the wake of bad pharmacology (delavirdine) and bad marketing (nevirapine). But it causes serious neurologic side effects such as nightmares, depression, and suicidal ideation that can make it difficult to tolerate. It must be taken on an empty stomach, meaning one hour before a meal, or two hours after a meal. Given other available options, Sustiva is not an obvious first choice for most people nowadays. If your provider recommends Sustiva, they may have a good reason, but make sure they tell you what it is.

Atripla, Symfi, and Symfi Lo (see those pages).

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

Average Wholesale Price
Sustiva 600 mg, 30 tablets:
$1,176.74/month
generic: 600 mg, 30 tablets:
$1,073.18/month
generic: 200 mg, 90 tablets:
$1,059.07/month
generic: 50 mg, 30 tablets:
$88.31/month
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 (Intence tablets are “chaky”) 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, or use frequently if adverse on drug reactions are comparable to those observed in adult subjects, except for rash, which was observed more frequently. In ages 6 to 18, rash of moderate intensity or greater (Grade 2 or greater) was reported more frequently in girls than boys (20.3% versus 5.4%). Half of the children 2–6 years old experienced at least a 20% decrease in the drug absorption and may need to have drug resistance before taking Intence. The TRIO study reported the combination of Intence with Prezista/Norvir and Isentress in highly treatment-experienced people was successful in getting many people to unde-
tectable. Some people 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 using etravirine in treatment-naive people who are pregnant. Individuals who become pregnant while taking etravirine may improve patient adherence. Although the DHHS recommen-
dation for Intence specifies drug resistance strains before taking it, the drug label does not—you do not need to have drug resistance before taking Intence. The PK data demonstrated that exposure to total etravirine was generally higher during pregnancy compared with post-
partum levels. Etravirine is known to have a variable (moderate to high) level of transfer across the human placenta, although insufficient data exist to evaluate the effects on a fetus. Pregnant individuals can vol-
untarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO aregistry.com.

**MARCH+APRIL 2022 | positivelyaware.com/intence**
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 people 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 comorbidities, 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, Stavudine, Zidovudine, 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 levels of Selzentry, such as Atripla, Sustiva, Inteleone, 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 (Harvoni) may have potential to increase Selzentry levels. Tell your provider or pharmacist about all medications, herbs, 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 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 (Trogarzo, Trofile DNA, or HIV-1 Coreceptor Tropism with Reflex to UDS) is needed to determine if this medication will work. Results of a phenotypic tropism test (Trogarzo or Trofile DNA) may take up to a month to complete. Genotypic tests are available and provide a faster and a less expensive alternative. Learn about Selzentry’s mechanism of action at youtube.com/watch?v=oneY0hG4aG0. Selzentry only works for people with CCR5-tropic virus. Viral tropism refers to the tropism of HIV that a person can have, CCR5 (R), CXCR4 (X4), or Dual-Mix Tropic (R and X4). Selzentry blocks CCR5, a co-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. ViV 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-naive individuals who are pregnant. Anyone who becomes pregnant while taking maraviroc may continue if viral suppression is effective and the regimen is well tolerated. 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 effects on a fetus. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO APREGISTRY.COM.

### AVERAGE WHOLESALE PRICE

150 mg pills:
- $1,659.70/month
- 300 mg, 60 tablets:
- $1,959.70/month

generic: price not available at press time

### MANUFACTURER

ViV Healthcare
vivihc.com; selzentry.com
(877) 844-8872

POSITIVELY AWARE 2022 HIV DRUG GUIDE
### 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 for subsequent doses. A Biologics License Application (sBLA) was submitted to the FDA in December 2021 for approval of an IV push formulation that administers undiluted Trogarzo over 30 seconds. Intramuscular administration is also being studied. Trogarzo must be given with an optimized background regimen (OBR). An OBR consists of the best antiretroviral therapy that can be selected for a patient based on the patterns of HIV drug resistance of their virus. Other considerations can include safety profile, tolerability, and lack of adverse drug-drug interactions or cross-resistance. 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 soon as possible. Then resume maintenance dosing (800 mg) every 14 days thereafter.

### POTENTIAL DOSE 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 who have multidrug resistance, along with an optimized background regimen (OBR). Go to bit.ly/Trogarzo-mechanism-of-action to watch a YouTube video of its mechanism of action. 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: “People with ongoing detectable viremia [detectable viral load] who lack sufficient treatment options to construct a fully suppressive regimen [get to undetectable plasma viral load] must be candidates for the recently approved [in 2018] 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. People must be on time. It is expensive because the cost of the drug is in addition 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 people 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. Other long-acting HIV drugs are on the way, however, and may be studied in combination with Trogarzo as well. Trogarzo is also the first HIV orphan drug—one that is produced for a relatively small population of people, fewer than 200,000. It was produced for people with multidrug-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 multidrug resistance, and have, therefore, limited treatment options. Trogarzo has been shown to work against highly drug-resistant virus, when combined with an OBR. Data presented at ID Week 2020 showed evidence for long-term safety and efficacy as well as tolerability in people receiving Trogarzo for almost a decade. Trogarzo has also demonstrated CD4 improvements in clinical studies.

As a biologic, IBA is the first HIV medication produced in cells rather than from chemicals. This does not make Trogarzo better, just different. 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. Most HIV drugs target parts of HIV, which are variable and thus susceptible to resistance. 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 works against multidrug-resistant HIV. It requires intravenous infusions every 2 weeks, and at a wholesale acquisition cost of $9,896 per month, is the most expensive antiretroviral drug ever approved. Administration costs are not included. Nonetheless, the egregious pricing is accompanied by a patient assistance program that protects people—if not the healthcare system—from much more expensive antiretrovirals. Still, the drug can be a lifesaver for people with multidrug-resistant virus who cannot otherwise construct a viable regimen. It has no known drug-drug interactions.

### ACTIVIST MICHAEL BRODER:

Trogarzo (ibalizumab) is the first drug in a new class called CD4-directed post-attachment inhibitor. Trogarzo blocks the virus from entering CD4 cells. Trogarzo is for use only in highly treatment-experienced people, meaning those who have already been on treatment for some time and have virus that is resistant to multiple HIV drugs. People using Trogarzo have virtually no other treatment options. More convenient oral or injectable HIV drugs are in development to treat multidrug-resistant virus in highly treatment-experienced people; but until those drugs are fully evaluated and approved, Trogarzo remains an important tool in the antiretroviral toolbox.

Thera Patient Support can assist with private or government insurance coverage, including AIDS Drug Assistance Program (ADAP), and will also assist in applying for the pharmaceutical co-pay assistance. Commercially insured people 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.

### MANUFACTURER

TaiMed USA

### DISTRIBUTED BY

Theratechnologies Inc. theratech.com; trogarzo.com

### AVERAGE WHOLESALE PRICE

$3,211.20 per box (2 vials); 10 vials for loading dose and four vials for continuing dose (every two weeks)

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**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 reaction formulated 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 efficacy or pharmacokinetics of Trogarzo. Based on animal data using higher doses of medication than would be used in humans, the FDA updated the drug label last year to include the potential for transient immunosuppression in infants exposed to the drug in the womb. See Section 8.1 (Pregnancy) in the prescribing information for more details.
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 in 2020, the most common side effect was nausea in 10% of study participants. Other side effects, observed less often, were diarrhea and fatigue. Use with caution in people 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 people without a history of liver disease.

■ POTENTIAL DRUG INTERACTIONS

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 anticycobacterial 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 that 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 (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 (the lowest possible starting dose for statins and monitor for statin-associated adverse effects). 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 on an as-needed or 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 of your past and present 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

Fostemsavir is the most expensive oral HIV drug with a wholesale acquisition cost of $7,650 per month, likely due to the relatively small market for the drug. There is a patient assistance program that makes the drug affordable to people while allowing ViiV to keep the price egregiously high. Fostemsavir should not be used in pregnancy due to insufficient safety data.

ACTIVIST MICHAEL BRODER: Approved in 2020, Rukobia (fostemsavir) is the first drug in a new class called a gp120-directed attachment inhibitor. Rukobia blocks the virus from entering CD4 cells. Rukobia is for use only in highly treatment-experienced people, meaning those who have already been on ART for some time and have virus that is resistant to multiple HIV drugs. Rukobia is one pill once a day with or without food. Rukobia must be used in combination with other HIV drugs, called an optimized background regimen (OBR). The OBR varies from person to person, based on the precise pattern of drug resistance of their virus. People using Rukobia have virtually no other treatment options. More convenient oral or injectable HIV drugs are in development to treat multi-drug-resistant virus in highly treatment-experienced people; but until these drugs are fully evaluated and approved, Rukobia remains an important tool in the HIV treatment toolbox.

DR. MELANIE THOMPSON: Fostemsavir, the prodrug of the active entity temsavir, is the first-in-class oral attachment inhibitor that prevents HIV from entering the T cell to establish permanent residency. It is approved only for treatment-experienced people, and is active against virus that is resistant to all other classes. The drug must be taken twice daily, but is well tolerated in general, with nausea being the most common side effect. There are a few drug-drug interactions which are contraindications to administration with the androgen receptor inhibitor enzalutamide, some seizures and tuberculosis medicines, mitotane, and St. John’s wort. Temsavir can increase plasma concentrations of the hepatitis C drugs grazoprevir and voxilaprevir, the oral contraceptive ethinyl estradiol (a maximum dose of 30 mcg is recommended), and most of the statins.

Fostemsavir was taken with ibalizumab by a handful of people in the BRIGHT study, but for some people with less advanced drug resistance, fostemsavir might offer an alternative to drugs such as ibalizumab or enfuvirtide.

Fostemsavir is the most expensive oral HIV drug with a wholesale acquisition cost of $7,650 per month, likely due to the relatively small market for the drug. There is a patient assistance program that makes the drug affordable to people while allowing ViiV to keep the price egregiously high. Fostemsavir should not be used in pregnancy due to insufficient safety data.

MANUFACTURER

ViiV Healthcare

ViiVhealthcare.com; rukobia.com

(877) 844-8872

AVERAGE WHOLESALE PRICE

$9,633.49/month

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positivelyaware.com
Apretude is the first-long-acting PrEP
(Pre-exposure Prophylaxis) for the prevention of HIV.

**STANDARD DOSE**
For HIV-negative adults and adolescents (male, female, and transgender) weighing at least 77 pounds (35 kg) for the prevention of HIV. One long-acting intramuscular gluteal (butt muscle) 600 mg injection (3 mL) monthly for the first two months and then one injection every 2 months thereafter. No food restrictions.

Daily oral lead-in therapy for about a month is optional before injections begin, consisting of a 30 mg tablet of Vocabria. Initiate injections on the last day of oral lead-in. Individuals who were on daily oral PrEP with Descovy or Truvada can transition directly to Apretude injections once their HIV-negative status is confirmed. Oral lead-in is used to determine tolerability. If up to 8 weeks of treatment is missed (less than or equal to 2 months), restart injections with the 600 mg dose of CAB LA as soon as possible, and then dose every 2 months thereafter. If more than 8 weeks of treatment site reaction was as soon as possible, followed a month later with another 600 mg dose, and then dose every 2 months thereafter. The oral medication can also be used as “bridging” if shots cannot be obtained on time—see package insert for instructions on planned and unplanned missed injections. The effect of severe liver impairment on cabotegravir is unknown. Longer needles, two inches (not included in the dosing kit), may be required for people with a higher BMI (body mass index) of 30 or more. Providers should follow directions for administration. (See Section 2.7 of package insert.)

**POTENTIAL SIDE EFFECTS AND TOXICITY**
The most common adverse reactions observed in 4% or more of people in clinical trials were injection site reactions (84%, with 59% having at least Grade 2—moderate—reactions), pyrexia (includes feeling hot, chills, and flu-like symptoms), fatigue, headache, and diarrhea. Hepatotoxicity has been reported in people with and without previous known liver problems or risk factors. Depressive disorders have been reported with Apretude and should be monitored. People given injections should be observed for at least 10 minutes afterwards to monitor for potential reactions. Individuals with pain from injections can use an ice pack or heating pack, and are advised to stretch and remain active. It is not recommended to overly massage the area. Monitor for signs of hypersensitivity, including elevated liver transaminases, and treat as needed.

**POTENTIAL DRUG INTERACTIONS**
Cabotegravir is contraindicated with rifampicin, rifapentine, carbamazepine, oxcarbazepine, phenytoin, and phenobarbital. It is recommended to co-administer rifabutin with caution because rifabutin can moderately increase the metabolism of cabotegravir and reduce its plasma level. It is not recommended to co-administer with cabotegravir. The effect of feminizing medications and hormones such as spironolactone and estrogens is not known. The use of hormonal contraceptives is not expected to have any significant effect on cabotegravir levels or protective effect. Methadone dose may need to be adjusted. Tell your provider or pharmacist about all medications, herbs, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions that are not listed here.

**MORE INFORMATION**
Approved by the FDA on December 20, 2021, Apretude is the first-ever long-lasting injectable PrEP medication—dosed just once a month for 2 months and then every other month thereafter. New onset reactions are highly desirable—different strokes for different folks. According to PrEP guidelines from the U.S. Centers for Disease Control and Prevention (CDC), “Cabotegravir injections may be especially appropriate for people with significant renal disease, those who have had difficulty with adherent use of oral PrEP, and those who prefer injections every 2 months to an oral PrEP dosing schedule.” GO TO bit.ly/cdc-prep-guidelines-2021. The label notes that “Risk for HIV-1 acquisition includes behavioral, biological, or epidemiologic factors including, but not limited to, condomless sex, past or current STIs, self-identified HIV risk, having sexual partners of unknown HIV-1 viremic status, or sexual activity in a high prevalence area or network. Counsel individuals on the use of other prevention measures (e.g., consistent and correct condom use; knowledge of partner’s HIV-1 status; regular testing for STIs that can facilitate HIV-1 transmission).” Advice on preparing for injection site reactions is included along with two important counseling points: the risk of developing drug resistance if HIV is acquired after stopping medication and the drug is still leaving the body, and the importance of keeping up follow-up appointments if stopping PrEP for any reason (page 51). The costs of taking HIV PrEP, which includes the costs of two clinical trials comparing Apretude to Truvada for PrEP. One trial enrolled men and transgender women who have sex with men and have high-risk behavior for HIV. The other trials enrolled cisgender women at risk of acquiring HIV. Both studies found Apretude to be superior to Truvada in preventing HIV infection.

**FDA approved for the prevention of HIV**

DR. MELANIE THOMPSON:
One of the most exciting developments of 2021 was the approval of injectable cabotegravir as PrEP. Given once every two months after an initial two injections given one month apart, Apretude was superior to oral Truvada in preventing new HIV infections for gay and bisexual men and transgender women, and for cisgender women.

Side effects included injection site reactions, headache, fever, fatigue, back pain, myalgia, and rash, including viral reactions were very common but rarely caused people to stop taking the drug.

My editorial comment here is that this could be a revolutionary step that improves adherence to treatment for people who don’t want injections. But there are some major caveats. I can only echo the masterful statement by Treatment Action Group: “In order for this new PrEP option to maximally contribute toward ending the U.S. HIV epidemic, we must develop and fully utilize additional intervention studies, demonstration projects, and sociobehavioral science studies that address unique barriers to access for all major vulnerable populations—including transgender and gender-nonconforming people; Black, indigenous, Latinx and other communities of color; cisgender women; people who use drugs; and people living in the Southern U.S. and rural communities, which are generally underserved by HIV prevention services relative to urban areas.”

While oral PrEP must be provided without out-of-pocket costs for people due to its “A” rating from the U.S. Preventative Services Task Force (USPSTF), at the time of publication, USPSTF decisions on the coverage for CAB PrEP were still pending. I will just say that this is a make-or-break moment for PrEP in the U.S. and to facilitate uptake with long-acting PrEP, its administration costs and associated labs (including STI screening) must be fully covered without cost sharing.

ACTIVIST MICHAEL BRODER: People can either start PrEP with Apretude or take oral cabotegravir (Vocabria) for one month to make sure they have no side effects that would prevent them from taking Apretude. The approval of Apretude is based on results from two clinical trials, comparing Apretude to Truvada for PrEP. One trial enrolled men and transgender women who have sex with men and have high-risk behavior for HIV. The other trials enrolled cisgender women at risk of acquiring HIV. Both studies found Apretude to be superior to Truvada in preventing HIV infection.

**MARCH+APRIL 2022**

**MANUFACTURER**
ViiV Healthcare
viivhealthcare.com
(877) 844-8972

**AVG WHOLESALE PRICE**
$4,440 per vial, based on WAC
Descovy for PrEP
		extamicitbine/tenofovir alafenamide
		FTC/TAF

Pre-exposure prophylaxis (PrEP)

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.

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 to FDA approval of Descovy for PrEP. There was also nausea (4%) and vomiting (1%). Descovy and other PrEP medications are not associated with 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 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 at the primary analysis). 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 compared to TDF (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 periodically for individuals 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 preexisting 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, TAF 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 Eplucsa. 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, herbs, and supplements you are taking or thinking of taking, prescribed or not.

MORE INFORMATION
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 population. A large study using Descovy for PrEP in cisgender women and adolescent girls, called PURPOSE-1, is 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. 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 people who may be at higher risk for renal and bone toxicity (including youths and older individuals). Insurers must now cover PrEP and its associated services (such as STI testing) without cost (such as co-pays) to people, but the details of coverage can vary. This is as a result of the Grade A recommendation from the U.S. Preventative Services Task Force (USPSTF). 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 prelocator.org and aidsvu.org—although any provider can prescribe.

FDA approved for the prevention of HIV

DR. MELANIE THOMPSON: Descovy was studied in cisgender gay and bisexual men and transgender women in the DISCOVER trial and found to be noninferior to Truvada as PrEP. Descovy was associated with lower rates of biomarkers of kidney toxicity, less bone density loss, and more weight gain, and higher LDL and HDL cholesterol than Truvada. Descovy is most valuable among people who are older or who already have or are at high risk for kidney toxicities or osteopenia/osteoporosis. As with Truvada, people with hepatitis B may experience flairs if Descovy is stopped without other drugs on board to treat hepatitis B.

【My editorial comment: This influential controversial trial (full disclosure: I was an investigator) showed robust community engagement in trial design and execution should not be bypassed by sponsors. The exclusion of cisgender women, transgender women, and people who inject drugs worsens disparities and leaves an unacceptable void in oral PrEP options for these populations, some of which may be filled by injectable cabotegravir. (Note that a trial of Descovy is indeed beginning for cisgender women.) Luckily, Truvada and its generic options remain the first choice for PrEP for many people, including cisgender women who are pregnant or contemplating pregnancy, and the price is decreasing over time owing to generic competition.】

For individuals, there should be no out-of-pocket cost for the drug or PrEP services (office visits, lab monitoring including hepatitis C drugs Harvoni or Zepatier. Descovy should be 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, herbs, and supplements you are taking or thinking of taking, prescribed or not.

ACTIVIST MICHAEL BRODER: TAF may be safer than TDF for bones and kidneys. This is especially important for people under age 25, who are still actively developing bone, and for people who have mild to moderate kidney disease. On the other hand, TAF has a worse profile than TDF when it comes to cholesterol and weight gain. Providers will weigh the choice based on their experience, and on the needs of each patient.

Pre-Exposure Prophylaxis

For more information, go to cdc.gov/hiv/basics/prep.html. Gilead Sciences helps people work with their insurance, including pre-authorizations, as well as provides free PrEP to uninsured people who are eligible and co-pay assistance for insured individuals up to $7,200 a year; contact the patient assistance hotline 24/7 at (877) 505-6986, or go to gileadadvancingaccess.com. DHHS HIV guidelines have a section on using PrEP for periconception, antepartum, and postpartum periods. PrEP Facts: Re-Stitching HIV. Preventing Sex is a closed Facebook group for people interested in or currently on PrEP, and their allies. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider, go to aapregistry.com.

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

AVERAGE WHOLESALE PRICE
30-day blister pack: $2,446.60

For more information, go to descovyforprep.com.

POSITIVELY AWARE 2022 HIV DRUG GUIDE

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Truvada for PrEP
emtricitabine/tenofovir DF
FTC/TDF

Pre-exposure prophylaxis (PrEP)

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.

POTENTIAL SIDE EFFECTS AND TOXICITY
No new serious side effects were observed when Truvada was studied for HIV prevention in clinical trials. Some people may experience nausea, headache, stomach pain, or weight loss. Risk compensation (when people put themselves at greater risk for infection, such as among people with 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 hepatitis B virus (HBV). Flare-up of hepatitis may occur—talk to your provider before discontinuing. Screening and monitoring requirements include checking for STIs and for hepatitis B and C. Insurers must now cover PrEP and its associated services (such as STI testing) without cost to people (such as co-pays), but the details of coverage can vary. This is as a result of the Grade A recommendation from the U.S. Preventative Services Task Force (USPSTF). 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-briefly-jul-aug-2017. DHHS HIV guidelines have a section on using PrEP for periconception, antepartum, and postpartum periods. PrEP Facts: Rethinking HIV Prevention and Sex is a closed Facebook group for people interested in or currently on PrEP, and their caregivers. For more information, go to cdc.gov/hiv/basics/prep.html. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; go to apregistry.com.

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

TRUVADA contains lactose, which is a component of the capsule shell. For HIV-negative adults and adolescents weighing at least 77 pounds, one tablet contains 200 mg emtricitabine and 300 mg tenofovir disoproxil fumarate. Truvada can cause kidney toxicities. Truvada alone is not a complete regimen to treat HIV. Continuing with Truvada after acquiring HIV may lead to drug resistance and limit future antiviral options. If you stop Truvada, any benefits you might have received (such as a reduced risk of acquiring HIV) may be lost. Nausea, headache, stomach pain, and persistent or worsening bone pain are among the most common side effects attributable to Truvada in PrEP trials. A new study showed that Truvada prevents infections in people with lower kidney function than in those with higher kidney function, but the incidence of fractures was low and similar in both arms. Tenofovir levels are increased with the hepatitis C drug Harvoni (ledipasvir/sofosbuvir) and close monitoring of TDF-related toxicities is recommended.

For individuals, there should be no out-of-pocket cost for the drug or PrEP services (office visits, lab monitoring including STI testing) due to coverage from the U.S. Preventative Services Task Force. I have to say that we badly botched the rollout of PrEP in the U.S., with many people who could benefit still lacking access to PrEP, and disparities by race, ethnicity, and gender writ large. We should learn from these mistakes as we have yet another opportunity to introduce PrEP to America with the approval of injectable cabegrevir (see Apretude) and the chance to make all PrEP available at no cost to people who wish to take it.

ACTIVIST MICHAEL BRODER:
Truvada (approved for PrEP in 2012) has been supplanted by Descovy, which replaces the TDF in Truvada with tenofovir alafenamide (TAF). TAF may be safer than TDF for bones and kidneys. This is especially important for people under 25, who are still actively developing bone, and for people who have mild to moderate kidney disease. On the other hand, TDF may be better than TAF when it comes to cholesterol and weight gain. If your provider recommends Truvada for PrEP rather than Descovy, they may well have a good reason, but make sure they tell you what it is.
A potential complication of HIV, antiretroviral therapy, or growth hormone (GH) deficiency may cause a fat redistribution of adipose tissue known as lipodystrophy (a form of lipodystrophy). Abdominal lipodystrophy 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). Hard belly may be a confused term because excess visceral abdominal fat may be mistaken for 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 occurs 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 people 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 people who have a history of cancer or problems with blood sugar or diabetes, and should be discontinued in critically ill people.

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. People 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.

AIDS on antiretroviral therapy. Currently, what is indicated for the symptomatic relief of non-infectious diarrhea in adults with HIV/AIDS is the first, and only, anti-diarrheal approved for use in those with HIV/AIDS and on antiretroviral therapy.

Mytesi approval was based on a randomized, placebo-controlled study of 374 HIV-positive people who had about three watery stools per day and were on anti-HIV medicines. At study entry, people experienced an average of approximately 20 watery stools per week. To be considered a responder, watery stools had to be less than two or fewer per week, which occurred in 18% of Mytesi-treated people vs. 8% of placebo-treated people at 4 weeks. In an open-label extension phase of the study, about 50% of the people 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 diarrhoea 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 people 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 people 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 people 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.

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

**STANDARD DOSE**

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

**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 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.

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).

**CAP & PAP INFORMATION**

**MANUFACTURER**

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

**AVERAGE WHOLESALE PRICE**

6 mg: 7 injections (usually a one-week supply) $5,297.04
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

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.
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 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: bit.ly/hiv-cap-and-pap.

**COST-SHARING ASSISTANCE PROGRAMS (CAP)**

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<tr>
<th>DRUGS COVERED</th>
<th>MANUFACTURER AND CONTACT INFORMATION</th>
<th>ASSISTANCE</th>
<th>RENEWAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kaletra and Norvir</td>
<td>AbbVie 800-441-4987, option 5; kaletra.com; norvir.com</td>
<td>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.</td>
<td></td>
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<tr>
<td>Atripla, Biktarvy, Compla, Descovy, Emtriva, Genvoya, Odefsey, Stribild, Truvada, Tybost, and Viread</td>
<td>Gilead Sciences 877-505-6986; gileadadvancingaccess.com</td>
<td>Biktarvy, Descovy, Genvoya, and Truvada: Covers the first $7,200 per year of co-payments. Compla, Odefsey, and Stribild: Covers the first $6,000 per year of co-payments. Emtriva: Covers the first $300 per month/$3,600 per year of co-payments. Tybost: Covers the first $50 per month/$600 per year of co-payments.</td>
<td>Rolls over on January 1</td>
</tr>
<tr>
<td>Edu rant, Intelence, Prezcobix, Prezi sta, and Symtuza</td>
<td>Janssen Therapeutics 866-836-0114; janssencarepath.com; edurant.com; intelence.com; prezista.com; prezcobix.com; symtuza.com</td>
<td>Covers the first $7,500 per year (for Symtuza, it’s $12,500) of co-payments, deductibles, and co-insurance.</td>
<td>Automatic renewal</td>
</tr>
<tr>
<td>Delstrigo, Isentress, Isentress HD, and Pifeltro</td>
<td>Merck and Co. 800-444-2080; isentress.com</td>
<td>Covers the first $6,800 of co-payments, deductibles, and co-insurance for each of 12 eligible prescriptions.</td>
<td>Enrollment is valid until coupon expires, 12/31/2021</td>
</tr>
<tr>
<td>Trogarzo</td>
<td>Theratechnologies 833-238-4372; trogarzo.com; therapatientsupport.com</td>
<td>Contact program for details Worked out on a case-by-case basis</td>
<td></td>
</tr>
<tr>
<td>Cabenuva, Dovato, Juluca, Lexiva, Rescriptor, Retrovir, Rukobia, Selzenty, Tivicay, Tivicay PD, Triumeq, Trizivir, Viracept, and Ziagen</td>
<td>Viiv Healthcare 844-588-3288; ViivVconnect.com</td>
<td>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, Selzenty, Trizivir, Viracept, and Ziagen: $4,800 per year/per patient maximum.</td>
<td>Automatic renewal</td>
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<tr>
<td>Invirase and Viread</td>
<td>Patient Access Network Foundation 866-316-7263; panfoundation.org</td>
<td>Maximum benefit is $3,600 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.</td>
<td>Reapply each year</td>
</tr>
</tbody>
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**PATIENT ASSISTANCE PROGRAMS (PAP)**

<table>
<thead>
<tr>
<th>DRUGS COVERED</th>
<th>MANUFACTURER AND CONTACT INFORMATION</th>
<th>FINANCIAL ELIGIBILITY</th>
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<tr>
<td>Kaletra, Norvir</td>
<td>AbbVie 800-222-6885 kaletra.com; norvir.com (co-pay information only); abvviepaf.org</td>
<td>Kaletra: 600% FPL ($77,280) Norvir: No income limits</td>
</tr>
<tr>
<td>Aptivus, Viramune XR</td>
<td>Boehringer Ingelheim 800-556-8317; boehringer-inglesheim.us</td>
<td>500% FPL ($64,400)</td>
</tr>
<tr>
<td>Atripla, Biktarvy, Complera, Descovy, Emtriva, Genvoya, Odefsey, Stribild, Truvada, and Tybost</td>
<td>Gilead Sciences* 800-226-2056 gileadadvancingaccess.com</td>
<td>500% FPL ($64,400)</td>
</tr>
<tr>
<td>Edurant, Intelence, Prezcobix, Prezista, and Symtuza</td>
<td>Janssen Therapeutics 800-652-6227; jjpaf.org</td>
<td>300% FPL ($38,640)</td>
</tr>
<tr>
<td>Delstrigo, Isentress, Isentress HD, and Pifeltro</td>
<td>Merck and Co. 800-727-5400 merckhelps.com; isentress.com</td>
<td>500% FPL ($38,640)</td>
</tr>
<tr>
<td>Trogarzo</td>
<td>Theratechnologies 833-238-4372; trogarzo.com</td>
<td>Call program for details</td>
</tr>
<tr>
<td>Cabenuva, Combivir, Dovato, Epivir, Epzicom, Lexiva, Juluca, Rescriptor, Retrovir, Rukobia, Selzentry, Tivicay, Triumeq, Trizivir, Viracept, and Ziagen</td>
<td>ViiV Healthcare 844-588-3288; ViivVConnect.com</td>
<td>500% FPL</td>
</tr>
</tbody>
</table>

* 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).

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**FOUNDATIONS**

**PROVIDING ACCESS TO CARE ASSISTANCE FOR PEOPLE LIVING WITH HIV**

- **Harbor Path**
  [harborpath.org](http://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](http://panfoundation.org) (866) 316-7263
  Provides necessary healthcare treatments to the underinsured population.

- **Patient Advocate Foundation**
  [patientadvocate.org](http://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.

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**ADDITIONAL RESOURCES**

**THESE MAY BE OF INTEREST TO INDIVIDUALS LIVING WITH HIV**

- **Clinical Trials**
  [clinicaltrials.gov](http://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](http://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](http://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](http://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](http://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.
I fractured my wrist in January while playing tennis. Though the pro with whom I was having a lesson was certainly distracting enough to be the cause, the fact is I was moving quickly to my right to pick up a forehand and tripped over my own feet. I rolled my right ankle and went down hard, my left hand reflexively deployed to break my fall. The racquet went flying, and I involuntarily issued a declaration of pain.

I popped up quickly and was walking off the rolled ankle. The wrist, I could feel, was not going to resolve itself as quickly. Nonetheless, wanting to appear tough and resilient to the hot, young pro, I said I would be okay, took a couple of ibuprofen, and finished the lesson—now focused entirely on my forehand so I did not need to use my left arm.

The wrist swelled up by the time the lesson finished, so I took more ibuprofen and iced it over the next 24 hours. Within a couple of days the swelling was down, and I thought it was just a bad sprain. But because it still wasn’t feeling great a week later—and I wanted to get back on the tennis court—I went to see my primary care doctor. He ordered an x-ray and, sure enough, it was an impaction fracture of the distal radius.

Shortly after it was diagnosed as a fracture, a friend—who knows my status but knows nothing about HIV medicine—asked if any of the medications I took affected my bone density. Duh! Of course I do—why hadn’t I thought about that? It has long been known that one side effect of tenofovir disoproxil fumarate (TDF) is reduced bone density. I took some form of TDF—first as Viread, then as a component of Atripla—for about 12 years. And about seven years after I started taking it, I broke a finger playing volleyball (apparently, while I like to play sports I am not very coordinated). This new wrist fracture has certainly given me reason to wonder whether TDF has reduced my bone density and made me more prone to fractures.

Even if I discover that my bone density has been reduced and may be a contributing factor to these fractures, I don’t have regrets about utilizing these medications to treat my HIV. All of the medications available at the time had side effects, and I am sure I was made aware that reduced bone density was one possible side effect from TDF. I needed medication to keep my HIV suppressed, and this was the choice my doctor and I made given the relative merits of the available options.

However, we now know that in 2004 Gilead shelved development of a version of tenofovir—tenofovir alafenamide fumarate (TAF)—that was effective at much lower doses and, therefore, had reduced side effects in terms of kidney function and bone loss. Years later, Gilead put TAF back into the development process, and it was approved by the FDA in 2015. It is now used in a variety of HIV medications, including the second approved version of PrEP (Descovy). In fact, the only real difference between Truvada and Descovy is the replacement of TDF with TAF, at a much lower dosage. In order to gain FDA approval for TAF, Gilead greatly touted the reduced effects on kidney function and bone loss.

This is the point at which all of this became a legal issue. You’ve probably seen the ads from personal injury firms seeking participants in the class actions against Gilead based on its conduct with respect to TDF and TAF. Those lawsuits allege that Gilead postponed development of TAF—a drug it knew would likely have reduced effects on kidney function and bone loss—in order to maximize its profits on TDF, which would be considered an inferior drug once TAF was approved. By delaying development and approval of TAF, the lawsuits allege, Gilead profited from TDF until its patent was about to run out and then replaced it with the new drug, for which the patent period was just beginning. In other words, just as Truvada was about to become available for manufacture in a generic form, Descovy—a safer version of PrEP that would be sold at non-generic prices—was approved. (Similarly, TAF replaced TDF in the HIV treatment drug Stribild, giving us Genvoya in November 2015.)

Gilead appears poised to reap the profits from TAF for many years to come. I am not an antitrust or patent lawyer (these are the areas of law at issue in the TDF/TAF lawsuits against Gilead), but these claims seem relatively solid to me. I will be interested to see whether Gilead’s claims that it temporarily shelved TAF for other reasons hold up in court. If they do not, an appropriate remedy would be for Gilead to cough up all TDF profits from the point at which TAF could have been approved (if Gilead had kept it in development) until it actually was approved. Some of that money could go to compensate people who took TDF and suffered adverse consequences, such as reduced kidney function or bone loss. Another portion of the money could go to provide free or low-cost Descovy to people who need it and can’t afford it.

The jury is still out on whether that first category of potential recipients includes me—I haven’t even had a bone density test yet—but Gilead should not profit from any intentional delay in developing a safer, more effective drug. That won’t heal my fractured wrist, but it would feel like justice served.

SCOTT SCHOETTES is an attorney and advocate who lives openly with HIV. 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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