HIV TREATMENT, PREVENTION + HEALTH FROM TPAN

POSITIVELY AWARE
MARCH+APRIL 2022

THE 26TH ANNUAL HIV DRUG GUIDE

APART, BUT TOGETHER

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

CONTRIBUTORS

THE PHARMACIST

Eric K. Farmer, PharmD, BCPS, AAHIVP, is an HIV clinical pharmacist at the Indiana University Health LifeCare Clinic at Methodist Hospital in Indianapolis, one of the largest providers of HIV medical services in the state of Indiana. He provides pharmacy services that include medication adherence counseling and patient education, drug information services, medication procurement, medication therapy management, and medical care coordination services. He is on the Board of Directors for the American Academy of HIV Medicine and serves as clinical faculty for the Midwest AIDS Training and Education Center. Dr. Farmer graduated from Butler University with his Doctor of Pharmacy in 2007. He then completed an ASHP-accredited PGY1 pharmacy residency at Eskenazi Health in Indianapolis, and subsequently an ASHP-accredited PGY2 HIV specialty pharmacy residency at the Center for HIV/AIDS Care and Research at Boston Medical Center.

THE DOCTOR

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

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

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

THE ACTIVIST

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.

THE ASSOCIATE EDITOR

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

THE EDUCATOR

Carla Blieden, PharmD, MPH, AAHIVP, completed her Doctor of Pharmacy, Master of Public Health, and PGY1 Residency at the University of Southern California. She is certified as an HIV pharmacist and has worked as the clinical pharmacist at the Maternal, Child, and Adolescent/Adult Center, a family-centered HIV clinic in Los Angeles, for over a decade. She works directly with patients focusing on adherence to HIV medication, managing other chronic diseases, and analyzing HIV medication resistance. Dr. Blieden has been working closely with City of Los Angeles officials and the Los Angeles Fire Department on deployment of the influenza and COVID vaccinations. Dr. Blieden is Assistant Professor of Clinical Pharmacy and Director of Student Outreach and Community Health at the USC School of Pharmacy. She reviewed the DHHS guidelines for this guide.

FARMER AND VÁZQUEZ: JOHN GRESS • BLIEDEN: ISAAC MORA

EDITOR'S NOTE

JEFF BERRY
@PAeditor

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.

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.

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)?

Problem solving involves looking at the problem, defining and analyzing the underlying concerns, then using your skills to facilitate change.

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.

PICOU: CHAD SAIN • WOMAN: SZEFEI-ISTOCK

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

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THIS MAGAZINE.

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EVERY ISSUE

'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**

FROM LEFT: ANDREA DE LANGE, DAWN McCLENDON, OLIVER WONG, ALFREDO "FREDDY" FAVELA, CARLOS MORENO, DANIELLE M. CAMPBELL, MPH, DAMONE THOMAS, MALLERY JENNA ROBINSON, ALICIA MOREHEAD-GEE, MD, JOSÉ MAGAÑA, AND NICHOLAS SNOW.

Apart, but together

BY **RICK GUASCO**

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.

"I learned of my status when I decided to get tested, despite the fear of being gay in Jamaica," he says. "Living with HIV motivates me to work in the field, to be at the table to help others living with HIV, and try to help people who are HIV negative to remain HIV negative.

"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

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engagement lead at UCLA's CARE Center.

In 2011, **Mallery ("Mally")Jenna 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 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 it. 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.

12 things to know about HIV

1. When should HIV treatment start?

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

2. What does HIV treatment do?

The goal of therapy is to suppress the amount of virus (called "viral load") to an undetectable level (meaning 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 naïve"), 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

treatment

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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."

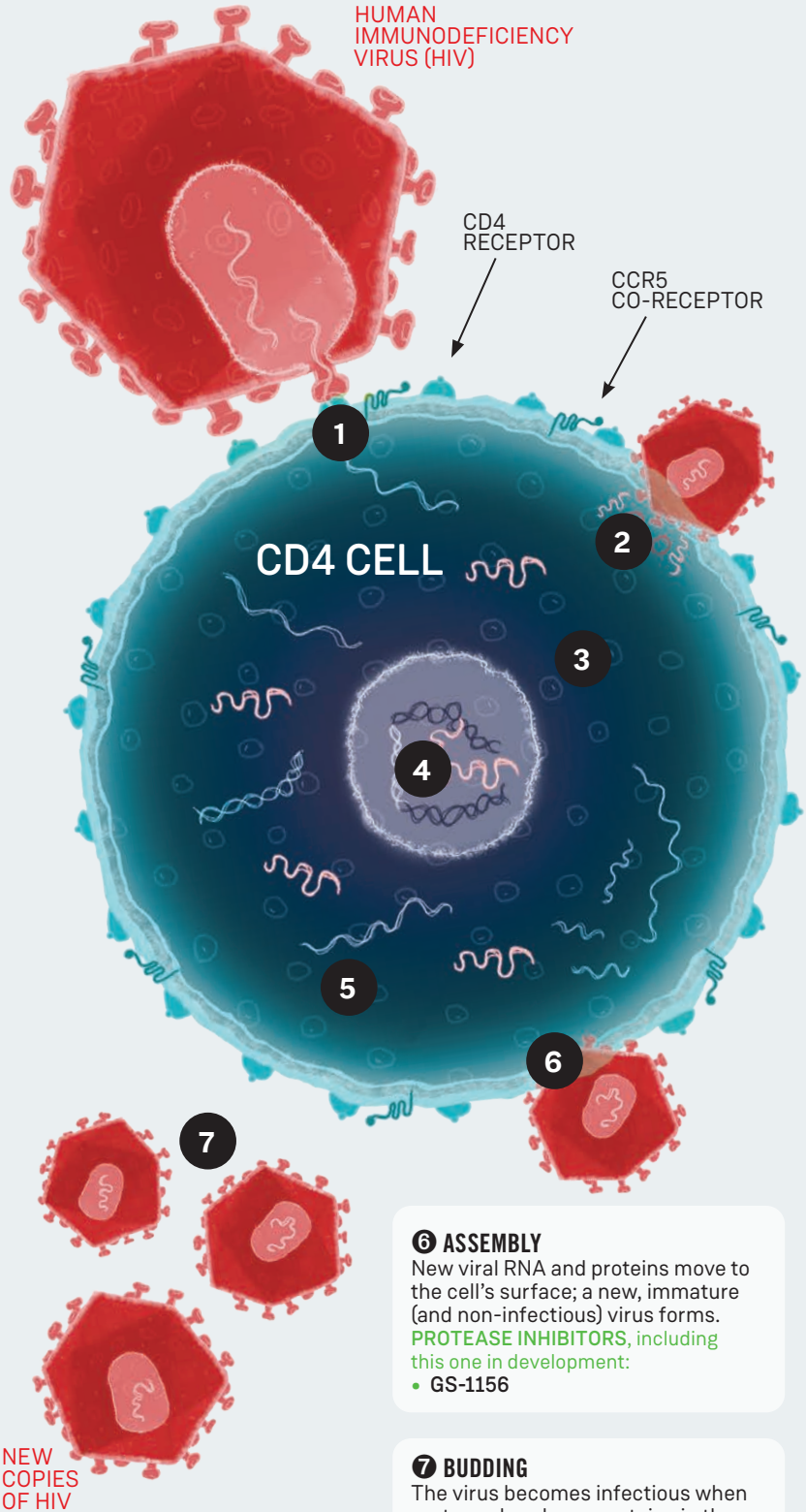
12. More information online

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.



❶ BINDING
HIV binds to the surface of a host cell.
ENTRY INHIBITORS

❷ FUSION
HIV's RNA reverse transcriptase, integrase, and other viral proteins fuse to the host cell.
FUSION INHIBITOR
MONOCLONAL ANTIBODIES (mAb) in development:
- **UB-421** (CD4 receptor)
- **VRC01** (CD receptor)
- **3BNC117/LS** and **10-1074/LS**
- **PGDM1400** and **PG121 10E8.4, etc.**
- **PRO-140** (CCR5 receptor)
- **albuvirtide**

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

NNRTIs, including these in development:
- **elsufavirine**

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

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

❻ ASSEMBLY
New viral RNA and proteins move to the cell's surface; a new, immature (and non-infectious) virus forms.
PROTEASE INHIBITORS, including this one in development:
- **GS-1156**

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

MATURATION INHIBITOR in development:
- **GSK3640254**

*** IN MARCH 2021, RESEARCHERS ACCEPTED THAT THE CAPSID UNCOATS IN THE NUCLEUS**

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

DHHS Guidelines for people starting HIV therapy for the first time

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

★ Recommended initial regimens for most people with HIV

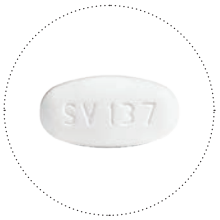
Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use.

INSTI + 2 NRTIs

Biktarvy
BIC / FTC / TAF
A1

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

INSTI + 1 NRTI



Dovato
DTG / 3TC
A1

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

INSTI + 2 NRTIs

Tivicay
DTG

WITH

Descovy
FTC / TAF

OR

Truvada
FTC / TDF

A1

✔ 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.

INSTI + 2 NRTIs

OR

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

WITH

Descovy
FTC / TAF
B2

OR

Truvada
FTC / TDF
B1

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

RATING OF EVIDENCE
1: Data from randomized controlled trials. 2: Data from well-designed non-randomized trials, observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies, or regimen comparisons from randomized switch studies. 3: Expert opinion.

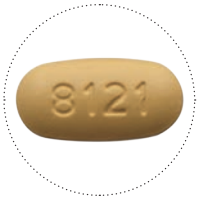
THE FOLLOWING ARE AVAILABLE AS CO-FORMULATED DRUGS
(NOT A COMPLETE LIST)

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

✔ Recommended initial regimens in certain clinical situations (continued)

Boosted PI + 2 NRTIs

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



Symtuza
DRV / COBI / FTC / TAF
B1

Prezcobix
DRV / COBI

OR

Prezista
DRV 800 mg

Norvir
RTV

WITH

Descovy
FTC / TAF

OR

Truvada
FTC / TDF

A1

Evotaz
ATV / COBI

OR

Reyataz
ATV

Norvir
RTV
B1

WITH

Descovy
FTC / TAF

OR

Truvada
FTC / TDF

Prezcobix
DRV/ COBI

OR

Prezista
DRV 800 mg

Norvir
RTV

B2

WITH

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

NNRTI + 2 NRTIs

Delstrigo
DOR / 3TC / TDF
B1

Pifeltro
DOR

WITH

Descovy
FTC / TAF

B3

✔ Recommended initial regimens in certain clinical situations (continued)

NNRTI + 2 NRTIs

3TC may substitute for FTC and vice versa

Atripla
EFV 600 mg / FTC / TDF
B1

Symfi
EFV 600 mg / 3TC / TDF
B1

Symfi Lo
EFV 400 mg / 3TC / TDF
B1

Sustiva
EFV 600 mg

WITH

Descovy
FTC / TAF

B2

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

Odefsey
RPV / FTC / TAF
B2

Complera
RPV / FTC / TDF
B1

Boosted INSTI + 2 NRTIs

Genvoya
EVG / COBI / FTC / TAF
B1

Stribild
EVG / COBI / FTC / TDF
B1

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

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

Dovato
DTG / 3TC
A1

Prezista
DRV 800 mg

+

Norvir
RTV

WITH

Isentress
(one tablet twice daily)
RAL

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

Prezista
DRV 800 mg

+

Norvir
RTV
C1

WITH

Epivir
3TC

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.

ADAPTED in part from HIV Pipeline 2021: New Drugs in Development, published by HIV i-Base, September 2021. Accessed online January 27, 2022. For the full report, **GO TO** i-base.info/htb/41142.

ALSO SEE HIV life cycle on page 12.

MARK HARVEY

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!

HIV & COVID-19

Statement about Paxlovid for people with HIV on antiretroviral therapy

Paxlovid is approved under Emergency Use Authorization to treat COVID-19 in persons at high risk for serious outcomes. It is a two-drug regimen of the protease inhibitors nirmatrelivir and ritonavir and is given twice daily for five days, beginning as soon as possible after diagnosis of COVID-19. As we know from decades of use in HIV treatment, ritonavir has many drug interactions that should be carefully considered before starting Paxlovid. A statement from the HIV Medicine Association of the Infectious Diseases Society of America recommends that people with HIV can take Paxlovid even if they are on a regimen containing ritonavir or cobicistat, but monitor for side effects. This is reiterated in the EUA package insert for Paxlovid. However, Paxlovid may interfere with other drugs you are taking, which would require holding other drugs temporarily or changing their dosage or, possibly, not taking Paxlovid. If you are going to take Paxlovid for COVID-19, be sure to tell your care provider about all the medicines you take, including those that are over the counter.

Statement from HIVMA and IDSA
idsociety.org/globalassets/covid-19-real-time-learning-network/patient-populations/hiv/oral-covid-tx-considerations-for-people-with-hiv-and-hcv.pdf

Statement from the COVID19 Treatment Guidelines
covid19treatmentguidelines.nih.gov/therapies/statement-on-paxlovid-drug-drug-interactions/

FDA Emergency Use Authorization Fact Sheet about Paxlovid
fda.gov/media/155050/download

Class list

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

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

PAGE	BRAND NAME	CATEGORY	GENERIC NAME
29	**Atripla**	STR	efavirenz/emtricitabine/tenofovir DF (EFV/FTC/TDF)
21	**Biktarvy**	STR	bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF)
31	**Cabenuva**	LA	cabotegravir/rilpivirine long-acting (CAB LA/RPV LA) injectable
41	**Cimduo**	NRTI*	lamivudine/tenofovir DF (3TC/TDF)
28	**Complera**	STR	rilpivirine/emtricitabine/tenofovir DF (RPV/FTC/TDF)
26	**Delstrigo**	STR	doravirine/lamivudine/tenofovir DF (DOR/3TC/TDF)
39	**Descovy**	NRTI*	emtricitabine/tenofovir alafenamide (FTC/TAF)
23	**Dovato**	STR	dolutegravir/lamivudine (DTG/3TC)
47	**Edurant**	NNRTI	rilpivirine (RPV)
43	**Emtriva**	NRTI	emtricitabine (FTC)
44	**Epivir**	NRTI	lamivudine (3TC)
42	**Epzicom**	NRTI*	abacavir/lamivudine (ABC/3TC)
36	**Evotaz**	PI / PKE	atazanavir/cobicistat (ATV/COBI)
27	**Genvoya**	STR	elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (EVG/COBI/FTC/TAF)
50	**Intelence**	NNRTI	etravirine (ETR)
34	**Isentress HD**	INSTI	raltegravir (RAL)
32	**lenacapavir**	CAI	lenacapavir (LEN)—NOT YET APPROVED AT PRESS TIME
24	**Juluca**	STR	dolutegravir/rilpivirine (DTG/RPV)
37	**Norvir**	PKE	ritonavir (RTV)
28	**Odefsey**	STR	rilpivirine/emtricitabine/tenofovir alafenamide (RPV/FTC/TAF)
48	**Pifeltro**	NNRTI	doravirine (DOR)
35	**Prezcobix**	PI / PKE	darunavir/cobicistat (DRV/COBI)
35	**Prezista**	PI	darunavir (DRV)
36	**Reyataz**	PI	atazanavir sulfate (ATV)
53	**Rukobia**	AI	fostemsavir (FTR)
51	**Selzentry**	EI	maraviroc (MVC)
27	**Stribild**	STR	elvitegravir/cobicistat/emtricitabine/tenofovir DF (EVG/COBI/FTC/TDF)
49	**Sustiva**	NNRTI	efavirenz (EFV)
30	**Symfi/Symfi Lo**	STR	efavirenz/lamivudine/tenofovir DF (EFV//3TC/TDF)
25	**Symtuza**	STR	darunavir/cobicistat/emtricitabine/tenofovir alafenamide (DRV/COBI/FTC/TAF)
41	**Temixys**	NRTI*	lamivudine/tenofovir DF (3TC/TDF)
33	**Tivicay**	INSTI	dolutegravir (DTG)
22	**Triumeq**	STR	dolutegravir/abacavir/lamivudine (DTG/ABC/3TC)
52	**Trogarzo**	EI	ibalizumab-uiyk (IBA)
40	**Truvada**	NRTI*	emtricitabine/tenofovir DF (FTC/TDF)
38	**Tybost**	PKE	cobicistat (COBI)
45	**Viread**	NRTI	tenofovir disoproxil fumarate (tenofovir DF, or TDF)
46	**Ziagen**	NRTI	abacavir sulfate (ABC)

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

HIV PREVENTION

57	**Apretude** for PrEP	PrEP	cabotegravir extended-release injectable suspension (CAB LA)
58	**Descovy** for PrEP	PrEP	emtricitabine/tenofovir alafenamide (FTC/TAF)
59	**Truvada** for PrEP	PrEP	emtricitabine/tenofovir DF (FTC/TDF)

NON-HIV DRUGS

60	**Egrifta SV**	tesamorelin for injection	for HIV-related hard belly fat
60	**Mytesi**	crofelemer	for HIV/AIDS-associated diarrhea
61	**Serostim**	somatropin for injection	for HIV-related wasting

Biktarvy

bictegravir/emtricitabine/tenofovir alafenamide
BIC/FTC/TAF

STR **Single-tablet regimen** containing an INSTI and two NRTIs

★ Recommended initial regimen for most people

STANDARD DOSE

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

For adults and children weighing at least 55 pounds (25 kg), 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 (bictegravir is not available separately).

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Most common side effects (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 initiation, 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 Temixys, Descovy, Emtriva, Epivir-HBV, Hepsera, Truvada, Vemlidy, or Viread, all for treatment of hepatitis B, as the emtricitabine and tenofovir components of Biktarvy already treat HBV. Biktarvy can be taken at least two hours before or six hours after taking laxatives or antacids, 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 Epclusa, Harvoni, Sovaldi, and Vosevi. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

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

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-380-4030, 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 3TC. Weight gain can be associated with INSTIs and TAF, and among INSTIs, bictegravir and dolutegravir were associated with more weight gain than elvitegravir/COBI, 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 defetilide 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.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$4,300.56/month

Triumeq

dolutegravir/abacavir/lamivudine
DTG/ABC/3TC

STR **Single-tablet regimen** containing an INSTI and two NRTIs

★ Recommended initial regimen for most people if HLA-B*5701 negative

STANDARD DOSE

One tablet once daily, without regard to food, for people with no evidence of INSTI resistance. 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.

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

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

POTENTIAL SIDE EFFECTS AND TOXICITY

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. 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 people with pre-existing psychiatric conditions. Conflicting data suggest people who have a high risk of cardiovascular problems have a potential for heart problems when using abacavir-containing regimens. Monitor for signs of hypersensitivity reaction (HSR) to abacavir. Prior to starting Triumeq, all individuals should be given a simple blood test to identify people at risk for this reaction. This test is covered by most insurance and by LabCorp/ViiV. Prior to initiation, test for hepatitis B virus (HBV). Severe exacerbations of HBV have been reported in people with co-infection who have discontinued Triumeq (due to elimination of the lamivudine component, which also treats HBV). 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 dofetilide. 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, Nexium, Pepcid, Prevacid, Prilosec, and Zantac) are okay to use. Avoid co-administration with oxcarbazepine, phenobarbital, phenytoin, or St. John's wort. Start metformin at lowest dose and titrate based on tolerability and clinical effect. Monitor for metformin adverse effects. Avoid use of sorbitol-containing medicines with lamivudine; there are many, such as acetaminophen liquid (Tylenol liquid and others). 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 dose. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions that are not listed here.

MORE INFORMATION

Triumeq has relatively few drug interactions and is well tolerated. Triumeq does not cover hepatitis B as well as other STRs and therefore requires another anti-HBV medication in addition to its lamivudine component. Triumeq is a relatively large STR tablet, which can potentially be an issue for individuals who have difficulty swallowing. Other STRs containing dolutegravir are Juluca and Dovato.

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

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$4,006.87/month

DR. MELANIE THOMPSON:

Triumeq is the only 3-drug INSTI-based STR not using a tenofovir base. This is helpful for people with renal or bone density abnormalities who can't take TDF or even TAF. The risk of abacavir hypersensitivity must be addressed with an HLA-B*5701 test prior to prescribing, therefore Triumeq cannot be used for rapid HIV treatment initiation.

Side effects common to all INSTIs may include insomnia or, rarely, worsening of depression or suicidal ideation, particularly if there are pre-existing mental health issues. Dolutegravir can be associated with weight gain, especially for women and African Americans. Keep track of your weight and pay attention to diet and exercise if you are starting Triumeq. There are concerns about using abacavir in persons with or with high risk for cardiovascular disease (see Ziagen). The DHHS panel recommends avoiding abacavir in persons with, or at high risk for, cardiovascular disease.

Drug interactions with dolutegravir are few but some are important. Do not take dofetilide or St. John's wort, and talk with your HIV care provider if you are taking metformin or medications for seizures or tuberculosis. For more info on drug interactions, see the comments about Tivicay. 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 Triumeq. (See Tivicay.)

ACTIVIST MICHAEL BRODER:

Triumeq (approved in 2014) cannot be taken by people who have a certain gene that makes them more likely to have a life-threatening allergic reaction to abacavir (your doctor will test you for the gene before prescribing Triumeq). Triumeq should not be taken by people with HBV. Concerns have emerged about weight gain on INSTI-containing regimens. As always, your provider should help you weigh the benefits against the risks.

Dovato

dolutegravir/lamivudine
DTG/3TC

STR **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-naïve people who have no known resistance to components of the regimen: dolutegravir and lamivudine. Tablet contains 50 mg of the INSTI dolutegravir plus 300 mg of the NRTI lamivudine.

Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. Dovato is not recommended for people who have severe liver impairment. According to the drug label, Dovato is not recommended for people with decreased kidney function (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 because of 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.

➤ SEE THE INDIVIDUAL DRUGS CONTAINED IN THIS MEDICATION: Tivicay and Epivir.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Dolutegravir and lamivudine are both generally well tolerated. Side effects occurring in at least 2% of study participants receiving Dovato included headache, nausea, diarrhea, insomnia, fatigue, and dizziness. INSTIs are associated with weight gain. Dolutegravir can cause a small, reversible increase in kidney function test (serum creatinine) within the first few weeks of treatment that does not affect actual kidney function. There have been rare reports of depression and suicidal ideation with INSTIs, primarily in people with a history of psychiatric illnesses. DHHS guidelines recommend closely monitoring people with pre-existing psychiatric conditions. Prior to initiation, test for hepatitis B virus (HBV). Severe exacerbations of HBV have been reported in people with HBV co-infection who have discontinued Dovato (due to elimination of the lamivudine component, which also treats HBV). Monitor liver enzymes closely. Initiation of HBV therapy may be warranted upon Dovato 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.

POTENTIAL DRUG INTERACTIONS

Do not take Dovato with Epivir-HBV. When taking carbamazepine or rifampin, take an additional dose of dolutegravir (in the form of one Tivicay tablet) 50 mg 12 hours after taking your Dovato dose. When starting or stopping dolutegravir by people on metformin, dose adjustment of metformin may be necessary to maintain optimal glycemic control or tolerability. Avoid use of sorbitol-containing medicines with lamivudine; there are many, such as acetaminophen liquid (Tylenol liquid and others). There are no known drug-drug interactions with Daklinza, Epclusa, Harvoni, Olysio, Sovaldi, Viekira Pak, or Zepatier. Not intended to be taken with other HIV medications, unless prescribed that way. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Approved in April 2019. Basically, this medicine is Triumeq without the abacavir component (brand name Ziagen, also found in Epzicom). Dolutegravir is from the powerhouse drug class of integrase inhibitors, which are highly effective and generally tolerable. The benefits of using a two-drug regimen for HIV include less exposure to HIV medication while maintaining viral suppression and minimizing the potential for side effects. At one, two, and nearly three years 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
viivhealthcare.com; dovato.com; (877) 844-8872

AVERAGE WHOLESALE PRICE

$3,182.63/month

DR. MELANIE THOMPSON:

The only two-drug regimen recommended for initial treatment, Dovato is great for some people, but shouldn't be taken if you have hepatitis B, resistance to 3TC/FTC, a viral load above 500,000 c/mL or, possibly, a CD4 count below 200/mL. Dovato isn't ideal for same-day treatment because a genotype or hepatitis B serology will not be available to guide choice of therapy. The TANGO study showed that, at 144 weeks, persons without prior treatment failure or hepatitis B whose virus is suppressed on a 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 when taken with dolutegravir, and a decrease in dolutegravir levels occurs with some seizure or tuberculosis medicines as well as St. John's wort and others. 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.

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). Concerns have emerged about weight gain on INSTI-containing regimens. As always, your provider should help you weigh the benefits against the risks.

Juluca

dolutegravir/rilpivirine
DTG/RPV

STR **Single-tablet regimen** containing an INSTI and an NNRTI

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

STANDARD DOSE

One tablet once daily, with a meal (see Edurant), for adults who are virologically suppressed (have an undetectable viral load of less than 50 copies per mL) on a current ART (antiretroviral therapy) regimen for at least 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 dose as soon as possible, with a meal, unless it is closer to the time of your next dose. Do not double up on your next dose. For proper absorption, rilpivirine must be taken with a meal that you chew—not just nutritional drinks or protein shakes.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Both dolutegravir and rilpivirine are generally well tolerated. Side effects observed in greater than 2% of study participants were diarrhea and headache. 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, Dexilant, Prilosec, Prevacid, Protonix, Nexium). Avoid taking Juluca with some seizure medicines (carbamazepine, oxcarbazepine, phenobarbital, and phenytoin) or St. John's wort. DHHS HIV treatment guidelines suggest that metformin be started at the lowest dose and titrated based on tolerability and clinical effect. Monitor for metformin adverse effects. When starting or stopping Juluca in people taking metformin, dose adjustment of metformin may be necessary to maintain optimal glycemic control. Not intended to be taken with other HIV medications, unless prescribed that way. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Juluca was the first two-drug combination approved as a complete regimen for HIV. It replaces a three- or four-drug therapy for people with undetectable viral loads who want to switch to a simpler or smaller tablet regimen. 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 may be advantageous to individuals who have difficulty swallowing. For individuals with HIV-2, commonly found outside the U.S., an NNRTI would not be recommended, as HIV-2 is inherently resistant to NNRTIs. Rilpivirine is an alternative drug for use during pregnancy, and although dolutegravir is now a preferred medication in pregnancy as well as for 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 apregistry.com.

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 its 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 tuberculosis. 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 sucralfate 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 recommended for initial treatment. If your provider recommends Juluca, they may have a good reason, but ask them what it is.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$3,755.30/month

Symtuza

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

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

✔ Recommended initial regimen in certain clinical situations

STANDARD DOSE

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

For adults and children weighing at least 88 pounds (40 kg). Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. Dose cannot be adjusted for people with kidney or liver problems. Symtuza can be used by people with an estimated creatinine clearance of at least 30 mL/min. It should not be used by people who have severe kidney or liver impairment. Symtuza is not recommended during pregnancy due to substantially lower exposures of darunavir and cobicistat components during pregnancy.

➤ SEE THE INDIVIDUAL DRUGS CONTAINED IN SYMTUZA: Prezista, Tybost, and Descovy.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

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 association 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 make these conclusions. With PIs, there can be increased bleeding in hemophiliacs. Cobicistat can cause a small, reversible increase in serum creatinine (SCr, which decreases estimated creatinine clearance) within the first few weeks of treatment without affecting glomerular filtration (the process by which the kidneys filter the blood; see Tybost for more information). While cobicistat does not affect actual kidney function, its effect on SCr can make monitoring of impaired kidney function more difficult or less accurate. However, people experiencing a confirmed increase in serum creatinine of greater than 0.4 mg/dL from baseline should be closely monitored for renal safety. Serum phosphorus in people with or at risk for kidney impairment should also be monitored. Prior to initiation, people should be tested for hepatitis B virus (HBV) infection. Severe exacerbations of hepatitis B have been reported in people co-infected with hepatitis B who have discontinued Symtuza (due to elimination of the emtricitabine and TAF components, which also treat 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 Symtuza discontinuation. Call your health care provider right away if you develop any of the following signs or symptoms of hepatitis: yellowing of the skin or whites of the eyes; dark or tea-colored urine; pale-colored bowel movements; nausea or vomiting; loss of appetite; or pain, aching, or tenderness on the right side below the ribs.

POTENTIAL DRUG INTERACTIONS

Do not take with alfuzosin, carbamazepine, dexamethasone, dronedarone, ergot derivatives, ivabradine, triazolam, oral midazolam, lomitapide, lurasidone, naloxegol, phenobarbital, phenytoin, pimozide, Revatio, simvastatin, lovastatin, St. John's wort, ranolazine, or rifampin. Monitor for lack of virologic response when eslicarbazepine or oxcarbazepine is necessary. Not recommended to be taken with avanafil, ciclesonide, dabigatran etexilate (in renal impairment), everolimus, Intelence, irinotecan, mometasone, rifabutin, rifapentine, rivaroxaban, salmeterol, ticagrelor, triamcinolone, or voriconazole. Beclomethasone, prednisolone, and prednisone as alternative corticosteroids may be considered, particularly for long-term use. Atorvastatin and rosuvastatin dose should not exceed 20 mg daily. Clinical monitoring is recommended with drospirenone, due to potential for hyperkalemia. Apixaban (Eliquis) dose may need to be adjusted. Do not take with colchicine if there is kidney or liver impairment. Initiation or dose adjustments of insulin or oral hypoglycemic medications may be required for some individuals. Cannot be taken with Zepatier. Based on the mechanism of action, drug interactions with other hepatitis C medications are probably similar to the interactions with Prezcobix + Descovy. Not intended to be taken with other HIV medications, unless prescribed that way. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions that are not listed here.

MORE INFORMATION

Symtuza is the first STR containing a protease inhibitor. This formulation is much more convenient and reduces the number of co-pays to one. It is not the same as Prezcobix plus Descovy, because Symtuza contains a lower dose of TAF than Descovy. A benefit of the PIs is their high genetic barrier to developing drug resistance. While medical providers may hate to say it out loud, this means greater forgiveness of missed doses; missing a dose here and there is never advisable but does happen. As such, a PI-based regimen such as Symtuza suits some people who may have trouble with the near-perfect drug adherence required of HIV treatment. In fact, the FDA allowed Janssen to advertise Symtuza as "help[s] protect against resistance." Symtuza may be used in rapid initiation treatment given within seven days of HIV diagnosis, before resistance test results are available. The DHHS recommendation, "in certain clinical situations," refers to concerns around adherence and the need for rapid initiation. Treatment-experienced individuals with undetectable viral loads for at least six months may switch to Symtuza. Compared with tenofovir DF, the tenofovir alafenamide in Symtuza is safer on kidney and bone health. Also as a result of the TAF, Symtuza can be taken by people with more advanced kidney disease, down to a renal function (CrCl) of 30 mL/min. Darunavir-containing regimens had stronger evidence supporting their use than do regimens containing atazanavir (the only other PI on the market). Darunavir regimens have an AI rating from DHHS ("A" for "strong" recommendation and the Roman numeral "I" for "data from randomized controlled trials") vs. a BI rating for atazanavir ("B" for "Moderate").

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

DR. MELANIE THOMPSON: 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 relatively small, open label study of Symtuza for rapid ART [antiretroviral therapy] initiation found high levels of viral suppression and low drug-related side effects, suggesting a potential use in this 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 darunavir 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 on Symtuza, talk with your HIV care provider about whether you should continue the drug.

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.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$5,150.92/month

Delstrigo

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

STR **Single-tablet regimen** containing an NNRTI and two NRTIs

✔ Recommended initial regimen in certain clinical situations

STANDARD DOSE

One tablet once daily without regard to food for people taking HIV treatment for the first time (treatment-naïve) or individuals with suppressed viral load on a stable HIV regimen for at least 6 months who have no known resistance to components of the regimen: doravirine, lamivudine, or tenofovir. Tablet contains 100 mg of the NNRTI doravirine plus 300 mg lamivudine and 300 mg tenofovir DF (TDF). Approved only for adults at this time.

Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. Dose cannot be adjusted for people with kidney problems; Delstrigo is not recommended for people with estimated creatinine clearance less than 50 mL/min. Should not be used by people with moderate or severe kidney impairment or severe liver impairment.

➤ SEE THE INDIVIDUAL DRUGS CONTAINED IN DELSTRIGO: Pifeltro, Epivir, and Viread.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

The most common adverse reactions observed with Delstrigo in clinical trials were dizziness (7%), nausea (5%), abnormal dreams (5%), and headache (4%). Neuropsychiatric events—such as depression, sleep disturbances, dizziness, etc.—are another common side effect of the NNRTI drug class. The proportion of people who reported one or more neuropsychiatric adverse events overall was 24% for the Delstrigo group compared to 57% for the Atripla group in the DRIVE-AHEAD study. Neuropsychiatric adverse events associated with depression and suicide/self-injury were reported in 4% of the Delstrigo group compared to 7% of the Atripla group. Overall, sleep disturbances (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 8% of those on Atripla. The doravirine component of Delstrigo did not appear to negatively affect cholesterol in studied populations. Decreases in bone mineral density (BMD) have been observed in people on TDF-containing regimens. BMD monitoring should be considered for people who have a history of bone fracture due to bone disease or are at risk for osteopenia or osteoporosis. TDF may cause kidney toxicities. Creatinine clearance (CrCl) should be assessed before initiating treatment. In addition to CrCl, glucose and protein in the urine and serum phosphorus should be monitored more often in people at risk for kidney problems. Tell your provider about any pain in extremities, persistent or worsening bone pain and fractures, with or without muscular pain or weakness, as well as any concerning changes in urinary habits, as these could be signs of kidney problems. Prior to initiation, people should be tested for hepatitis B virus (HBV) infection. Severe exacerbations of hepatitis B have been reported in people co-infected with 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, Emtriva, Epivir-HBV, Hepsera, Truvada, Vemlidy, or Viread, all used for hepatitis B. When using with the antibiotic drug rifabutin (used for TB and to prevent MAC in people with AIDS), increase the doravirine dose by adding a Pifeltro 100 mg tablet approximately 12 hours later. Avoid taking Delstrigo with drugs that negatively affect the kidneys, including chronic use or high doses of anti-inflammatory drugs for pain such as Advil or Motrin (ibuprofen) and Aleve (naproxen). The following medications may lower the blood levels of doravirine, and therefore may decrease its effectiveness, and should not be used with Delstrigo: the anticonvulsants carbamazepine, oxcarbazepine, phenobarbital, and phenytoin; the androgen receptor inhibitor enzalutamide; the antimycobacterials rifampin and rifapentine; the cytotoxic agent (a cancer drug) mitotane; and the herbal St. John's wort. Avoid using sorbitol-containing medicines with lamivudine; there are many, such as acetaminophen liquid (Tylenol liquid and others). Epclusa and Harvoni each increase the concentration of TDF; monitor for adverse reactions. Not intended to be taken with other HIV medications, unless prescribed that way. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions that are not listed here.

MORE INFORMATION

Stand-alone versions of doravirine (Pifeltro) and lamivudine/tenofovir DF (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 clinical trials yet. In the DRIVE-FORWARD study comparing doravirine to darunavir, at 96 weeks, 72% of treatment-naïve individuals in the doravirine group attained undetectable status (a viral load of less than 50 copies/mL), compared to 65% for the darunavir group. For individuals with HIV-2, commonly found outside the U.S., an NNRTI would not be recommended as HIV-2 is inherently resistant to NNRTIs. There are no data on the safe use of Delstrigo during pregnancy. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

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 (1.7 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.

Doravirine has fewer drug-drug interactions than either efavirenz or rilpivirine, but levels can be decreased by some seizure or tuberculosis medicines, St. John's wort, and enzalutamide, an androgen blocker. Initial hope that it might be genetically more robust and less likely to select for drug resistance, however, has been somewhat disappointing. Because none of the doravirine trials compared the drug to INSTIs, it isn't recommended as initial therapy for most people in the U.S., although the Europeans have elevated Delstrigo to first line in the recent EACS guidelines.

Delstrigo is not recommended in pregnancy due to insufficient data on safety.

ACTIVIST MICHAEL BRODER:

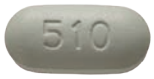
TDF, notorious for safety issues with bones and kidneys, has been kicked aside by its safer chemical cousin, tenofovir alafenamide (TAF). If your provider recommends Delstrigo, they may have a good reason, but make sure they tell you what it is.

MANUFACTURER

Merck & Co.
delstrigo.com
(800) 672-6372

AVERAGE WHOLESALE PRICE

$2,917.08/month



Genvoya

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

Stribild

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

STR **Single-tablet regimens** containing a boosted INSTI and two NRTIs

✔ Recommended initial regimens in certain clinical situations

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.

STRIBILD: 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 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. 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 Cimduo 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, alfuzosin, carbamazepine, phenobarbital, phenytoin, ergotamine, dihydroergotamine, methyl-ergonovine, oral midazolam, lurasidone, pimozide, Revatio, rifampin, rifabutin, rifapentine, Serevent, triazolam, St. John's wort, clopidogrel, or ticagrelor. Rosuvastatin and atorvastatin should be used with caution and started at the lowest 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 using 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 lowest 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, herbals, 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.

STRIBILD: 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.

DR. MELANIE THOMPSON: These STRs are no longer recommended for initial therapy for most people because elvitegravir requires a cobicistat booster, introducing many drug-drug interactions, and because of its genetic fragility compared to dolutegravir and bictegravir. The difference between them is that Genvoya uses TAF while Stribild uses TDF. Compared head-to-head, Genvoya was noninferior to Stribild up to 96 weeks, but Genvoya was superior at 144 weeks, although this was not a primary endpoint.

When taken together, TDF and COBI sometimes have been associated with kidney toxicity and low bone density, so close monitoring is important.

ACTIVIST MICHAEL BRODER: Gilead's rationale for developing Genvoya was to switch out an earlier incarnation of tenofovir (TDF) in Stribild for its safer chemical cousin (TAF). So far so good, but with newer options, scarcely anyone needs to be on a boosted anything these days, and the fact that elvitegravir needs cobicistat is a big downside.

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 apregistry.com.

MANUFACTURER

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

GENVOYA AWP

$4,300.56/month

STRIBILD AWP

$4,511.29/month

Odefsey

rilpivirine/emtricitabine/
tenofovir alafenamide
RPV/FTC/TAF

Complera

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

STR **Single-tablet regimens** containing an NNRTI and two NRTIs

✔ Recommended initial regimens in certain clinical situations

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/mm^3 before starting rilpivirine due to higher rates of virologic failure in these people. The CD4 requirement, however, is no longer on the drug label.

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

➤ SEE THE INDIVIDUAL DRUGS: 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.

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, aching, 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, Hepsera, Truvada, Vemlidy, or Viread, which are all used for the treatment of hepatitis B. Proton pump inhibitors (PPIs, heartburn or stomach acid drugs such as Aciphex, Dexilant, Nexium, Prevacid, Prilosec, Protonix, etc.) cannot be taken. Antacids containing aluminum, magnesium hydroxide, or calcium carbonate can be taken two hours before or four hours after Odefsey or Complera. Stomach acid-reducing drugs such as Pepcid, Tagamet, and Zantac can be taken 12 hours before or four hours after a dose of Odefsey or Complera. Do not take with carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifampin, rifapentine, or the herb St. John's wort. Do not take with more than one dose of the injectable steroid dexamethasone (sometimes given in the ER or hospital). Use caution if taken with fluconazole, itraconazole, ketoconazole, posaconazole, or voriconazole. Use azithromycin when possible instead of the antibiotics clarithromycin, erythromycin, or telithromycin, because these drugs increase rilpivirine levels, which can increase the risk of side effects. Reduced methadone levels can occur; 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 Zepatier, but Complera cannot. Odefsey can be taken with Epclusa, but monitor for tenofovir toxicity with Complera. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Odefsey is an option for people with impaired kidney function. For individuals with HIV-2, more commonly found outside the U.S., an NNRTI would not be recommended as HIV-2 is inherently resistant to NNRTIs. Pregnant individuals virologically suppressed on Odefsey or Complera may continue taking it. 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.

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 loads ≥ 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. 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; genvoya.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

Atripla

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

STR **Single-tablet regimen** containing an NNRTI and two NRTIs

✔ Recommended initial regimen in certain clinical situations

■ GENERIC IS AVAILABLE

■ STANDARD DOSE

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

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

Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. Do not split or crush the tablet. Dose cannot be adjusted for people with kidney problems; Atripla should not be used in people with moderate or severe kidney or liver impairment. Atripla is not recommended for people with CrCl less than 50mL/min or individuals requiring dialysis.

Similar, but not exact, medications are available (see Symfi and Symfi Lo).

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

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

■ POTENTIAL SIDE EFFECTS AND TOXICITY

Use with caution in individuals with depression or other psychiatric issues who are not receiving mental health care. A 2014 study reviewed four previously published AIDS Clinical Trials Group (ACTG) studies regarding efavirenz and suicidal ideation and re-emphasized an association between efavirenz and suicidality (reported suicidal ideation or attempted or completed suicide), and should be used with caution in 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 enzymes closely in people with co-infection. 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 Temixys, Descovy, Emtriva, Epivir-HBV, Hepsera, Truvada, Vemlidy, or Viread, all used for the treatment of hepatitis B. Avoid taking with drugs that negatively affect the kidneys, including chronic use or high doses of anti-inflammatory drugs for pain such as Advil or Motrin (ibuprofen) and Aleve (naproxen). Atripla should not be taken with voriconazole, ergot derivatives, midazolam, pimozide, triazolam, bepridil, or St. John's wort. Atripla should also not be taken with other medications that prolong QTc interval (a heart problem) or medications with a known risk for torsades de pointes. For 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 affect warfarin levels. Can decrease levels of buprenorphine and methadone—monitor for withdrawal. When taken with carbamazepine, phenobarbital, or phenytoin, periodic monitoring of anticonvulsant and efavirenz levels should be done or alternative anti-seizure drugs, such as levetiracetam, should be considered. Effectiveness of birth control pills may be decreased; consider using other contraceptive methods. Closer monitoring and dose adjustments may be required with posaconazole (avoid unless benefit outweighs potential risk) and itraconazole. Monitor effectiveness of clarithromycin or consider using azithromycin instead. Levels of immunosuppressants should be monitored when starting or stopping. Cardizem, Lipitor, Pravachol, and Zocor doses may need to be adjusted. Titrate dose of bupropion and sertraline based on clinical response. No dose adjustment of Atripla needed with Sovaldi. Use caution when administering Atripla with Harvoni, and monitor renal function closely due to possible increased tenofovir levels. Increase dose of Daklinza to 90 mg when used with Atripla. Atripla should not be taken with Epclusa or Zepatier. Not intended to be taken with other HIV medications, unless prescribed that way. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions 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 NNRTIs. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

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 EKG changes that could be associated with 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 3TC instead of FTC. 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 rapid pace of drug advances in HIV treatment. See Descovy and Truvada.

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 neurologic 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 worrisome bone and kidney side effects. Given other available options, it's hard to imagine why any provider today would recommend Atripla for any person requiring HIV treatment.

■ MANUFACTURERS

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

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

■ AVERAGE WHOLESALE PRICE

Generic is available:
$3,413.97/month

Symfi *and*  Symfi Lo

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

STR **Single-tablet regimens** containing an NNRTI and two NRTIs

✔ Recommended initial regimens in certain clinical situations

STANDARD DOSE

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

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

Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. Do not split or crush the tablet. Dose cannot be adjusted for people with kidney problems. Symfi and Symfi Lo are not recommended for 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.

- SEE THE INDIVIDUAL DRUGS contained in Symfi and Symfi Lo: Sustiva, Epivir, and Viread. See also similar STR, Atripla.
- SEE PACKAGE INSERT for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

The most common side effects 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). Severe exacerbations of HBV have been reported in people with HBV co-infection and have discontinued emtricitabine and/or tenofovir, both of which treat hepatitis B. Monitor liver enzymes closely in co-infection. Initiation of HBV therapy may be warranted upon discontinuation. 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. See Atripla. 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/Temixys, Descovy, Emtriva, Epivir-HBV, Hepsera, Truvada, Vemlidy, or Viread, all used for treatment of hepatitis B. Do not take with another nephrotoxic (harmful to the kidneys) medication, such as high-dose or multiple NSAIDs (non-steroidal anti-inflammatory drugs; these include aspirin, ibuprofen—Motrin, Advil, and others, and naproxen sodium—Aleve and others). Should not be taken with voriconazole, ergot derivatives, midazolam, pimozide, triazolam, bepridil, or St. John's wort. Efavirenz should also not be taken with other medications that prolong QTc interval (a heart problem) or medications with a known risk for torsades de pointes. For 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 decrease effectiveness of birth control pills; consider the use of other contraceptive methods. Closer monitoring and dose adjustments may be required with posaconazole (avoid unless benefit outweighs potential risk) and itraconazole. Monitor effectiveness of clarithromycin or consider using azithromycin instead. Levels of immunosuppressants should be monitored when starting or stopping Symfi or Symfi Lo. Cardizem, Lipitor, Pravachol, and Zocor doses may need to be adjusted. Titrate dose of bupropion and sertraline based on clinical response. Avoid use of sorbitol-containing medicines with lamivudine; there are many, such as acetaminophen liquid (Tylenol liquid and others). Use caution when administering with Harvoni and monitor renal function closely due to possible increased tenofovir levels. Should not be taken with Epclusa or Zepatier. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions that are not listed here.

MORE INFORMATION

Symfi and Symfi Lo are basically alternative versions of Atripla, a medication that's no longer preferred when starting therapy. The advantage is they may be a cheaper alternative than some first-line medications because their components are all available as generics. If you can't sleep, ask your doctor about gradually adjusting the timing of your dose until it's taken during the day. A genetic trait affecting drug metabolism of 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 associated with serious heart rhythm abnormalities (QTc prolongation). Efavirenz also has many drug-drug interactions that complicate its use with many 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 associated with fewer side effects. 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 rapid pace of drug advances in HIV treatment.

ACTIVIST MICHAEL BRODER: Symfi and Symfi Lo were approved in 2018, and are "branded 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. If your provider recommends Symfi or Symfi Lo, they may have a good reason, but make sure they tell you what it is.

Cabenuva

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

LA **Long-acting injectable regimen;** contains an INSTI and an NNRTI

✔ 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 (butt 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 dosing, continue with this dose for months 2 and 3, and then every other 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 Tables 4 and 5 of package insert for instructions on missed doses. 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.

DR. MELANIE THOMPSON: Cabenuva is the first complete injectable regimen for HIV treatment and can be given once 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 FLAIR study included 111 people who switched from oral DTG/ABC/3TC directly to injectable 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. ViiV 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 appointments every month or every two months. 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, tell 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, ViiV 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.

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

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

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Oral lead-in should be used to assess for safety and tolerability. The most common adverse reactions observed in 2% or more of people receiving Cabenuva in clinical trials were injection site reactions (83%, with 37% having at least Grade 2—moderate), pyrexia, fatigue, headache, musculoskeletal pain, nausea, sleep disorders, dizziness, and rash. Serious post-injection reactions reported within minutes of administration (in less than 1% of people injected) may have been associated with inadvertent (partial) intravenous administration and began to resolve within a few minutes after injection in clinical studies: difficulty breathing (dyspnea), abdominal cramping, agitation, flushing, sweating, oral numbness, and changes in blood pressure. Instructions for injection should be followed carefully to avoid accidental intravenous administration. People given injections should be observed for approximately 10 minutes afterwards to monitor for potential reactions. Individuals with pain from injections can use an ice pack or heating pack and are 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 a median weight gain of 3.3 pounds in Cabenuva trials.

POTENTIAL DRUG INTERACTIONS

Cabenuva is contraindicated with carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifabutin, rifampin, rifapentine, systemic dexamethasone (more than one dose), or the herb St. John's wort. Clinical monitoring of methadone is recommended because it may need to be adjusted in some people due to decreased levels. Macrolide antibiotics like azithromycin, clarithromycin, and erythromycin are expected to increase concentrations of rilpivirine and are associated with a risk of QT prolongation (these abnormal heart rhythms can make the heart stop) or possible torsade de pointes. Where possible, consider alternatives such as azithromycin, which increases rilpivirine concentrations less than other macrolides. See Edurant for oral lead-in. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Residual concentrations may remain in the body for more than a year after discontinuation. Therefore, it is essential to initiate an alternative, 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/m^2. People with a history of exposure to an NNRTI may consider obtaining a GenoSure Archive resistance test to assess archived mutations that may decrease the susceptibility to rilpivirine. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com. -

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

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

NOT YET APPROVED AT PRESS TIME

lenacapavir

lenacapavir
LEN

CAI **Long-acting capsid inhibitor**

● DHHS recommendation not established

STANDARD DOSE

Lenacapavir is a long-acting subcutaneous injection administered once every six months by a healthcare provider.

In the Phase 2/3 CAPELLA clinical trial for heavily treatment-experienced individuals, two 300 mg tablets were given on Day 1 and Day 2 and one 300 mg tablet was given on Day 8 as an oral initiation. On Day 15, a maintenance dose of 927 mg (two 1.5 mL injections) was administered by subcutaneous injection into the abdomen, and was then injected every six months thereafter.

Lenacapavir must be taken in combination with other antiretroviral(s).

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

POTENTIAL SIDE EFFECTS AND TOXICITY

In the CAPELLA study, 56% of participants (40 out of 72 individuals) had at least one injection site reaction (ISR). Most (70%) were Grade 1 (mild). There were no discontinuations for ISR. For Grade 3 and 4 abnormalities, four individuals (6%) experienced hyperglycemia (high blood sugar); four experienced glycosuria (excess sugar in urine); and eight individuals (11%) experienced low creatinine clearance (eGFR) or high creatinine—signs of kidney toxicity. The hyperglycemia, glycosuria, and creatinine changes observed were related to the individual's diabetes or was either transient or unconfirmed. No dose adjustment is anticipated for individuals with mild to moderate hepatic (liver) impairment or mild, moderate, or severe renal impairment.

POTENTIAL DRUG INTERACTIONS

Based on drug-drug interaction studies, lenacapavir should not be taken with Evotaz or the TB drug rifampin. Use caution with the sedative midazolam (Versed). Okay to take with Prezcobix, the antacid famotidine (Pepcid), the cholesterol drug rosuvastatin (Crestor), tenofovir alafenamide (TAF, found in Descovy and other medications), and the antifungal voriconazole. Other acid-reducing medications can be used, such as the H2 blockers (such as Axid, Tagamet, and Zantac) and proton pump inhibitors (including Nexium, Prevacid, and Prilosec). Clinical trials did not allow the use of atazanavir (Evotaz or Reyataz), efavirenz (Atripla, Sustiva, Symfi, or Symfi Lo), etravirine (Intelence), nevirapine (Viramune), or tipranavir (Aptivus); all other HIV medications were allowed. See prescribing information after approval for more information.

MORE INFORMATION

Lenacapavir was expected to be approved by the FDA this year. This long-acting subcutaneous injection —administered just once every six months—is the first in its drug class. It was granted a Breakthrough Therapy Designation by the FDA in 2019. Lenacapavir is a capsid inhibitor, and inhibits HIV replication by interfering with multiple essential steps of the viral lifecycle. Ultimately, it prevents viral RNA from entering the nucleus of human CD4 T cells, halting virus assembly and protein formation, and inhibiting assembly of new viral particles. The approval is anticipated for heavily treatment-experienced (HTE) individuals with resistance to multiple HIV drug classes. Lenacapavir is highly potent at low doses. Drug efficacy was similar across demographic groups (race, sex at birth, age, and geographic region), CD4 cell count and viral load at study entry, and which background HIV medications were used. Lenacapavir was studied as an injection taken every six months and must be used with an optimized background regimen (OBR). It is important that people still take other HIV medications in addition to lenacapavir. As always with HIV therapy, remember that adherence remains important for good results. Adherence may be an issue for some people whose HIV therapy has led to drug resistance—information and support is available. As a first-in-class medication, lenacapavir lacks cross-resistance to other HIV drugs.

Future drug development plans include lenacapavir-containing complete regimens to provide treatment options to individuals and use as a single drug for HIV prevention. HIV prevention studies with injectable lenacapavir taken once every six months for PrEP (pre-exposure prophylaxis) began last year. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; **GO TO** apregistry.com. There are two other drugs currently approved for HTE individuals, Rukobia (BRIGHT study) and Trogarzo (TMB-301) (see those pages). As a medication for HTE individuals with multiple drug resistance, lenacapavir is a much-needed drug for many people living with HIV who have limited treatment options

DR. MELANIE THOMPSON: 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 fostemsavir (Rukobia), 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 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, 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.

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.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

Lenacapavir was not yet on the market as this issue went to press

Tivicay

dolutegravir
DTG

INSTI Integrase strand transfer inhibitor

★ Recommended as a component of initial regimen for most people

STANDARD DOSE

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

For adults and children weighing more than 44 pounds (20 kg), use standard dose listed above or see package labeling. 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 those 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.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

In general, Tivicay is well tolerated with infrequent side effects. The most common moderate to severe side effects in clinical studies were insomnia (3%), headache (2%), and fatigue (2%). Mild insomnia was observed in 7% of participants in one study. Increased CPK (creatine 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.

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, Tivicay, Triumeq, Dovato, Cabenuva, and Juluca. Do not take with the anti-arrhythmic dofetilide. Intelence decreases Tivicay levels by 88%, therefore, these two medications must be co-administered with Kaletra, boosted Prezista, or boosted Reyataz. Tivicay should be taken two hours before or six hours after taking laxatives or antacids, the ulcer medication sucralfate, oral iron or calcium supplements, or buffered medications. It can be taken with iron- or calcium-containing supplements if taken together with food. Acid reducers (Pepcid, Zantac, Tagamet) and proton pump inhibitors (for example, Aciphex, Dexilant, Prilosec, Prevacid, Protonix, and Nexium) are okay to use. Avoid taking with Viramune, oxcarbazepine, phenytoin, phenobarbital, or St. John's wort. Start metformin at lowest dose and titrate based on tolerability and clinical effect. Monitor for metformin adverse effects. Use of rifampin, carbamazepine, efavirenz, Aptivus/Norvir, and Lexiva/Norvir in treatment-naïve or treatment-experienced, INSTI-naïve adults requires dosing Tivicay 50 mg twice daily. Tivicay may increase levels of the potassium channel blocker dalfampridine, which could increase the risk of seizures. No known interactions with Epclusa, Harvoni, or Zepatier. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions that are not listed here.

MORE INFORMATION

Tivicay is considered a second-generation INSTI—it may work in many individuals whose virus has developed resistance to other INSTIs, but they will need twice-daily dosing. Compared to other INSTIs, Tivicay has a high genetic barrier against 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 apregistry.com.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

50 mg tablets: **$2,413.66**/month

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 people.) The recommendation 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.

Side effects include weight gain, particularly in women and African Americans. Weight gain appears to be higher when DTG is taken with TAF. A pooled analysis found that persons on dolutegravir or bictegravir gained an average of 3.5 kg [7.7 lbs.] over 96 weeks. Rash has been seen with dolutegravir, as has liver toxicity, especially for people with hepatitis B or C. All INSTIs can cause insomnia or depression. Depression, including suicidal ideation, occurs most often in people with pre-existing mental health issues. By the way, dolutegravir increases blood creatinine levels by 0.15 mg/dL due to changes in tubular secretion in the kidneys without any actual kidney damage.

Dolutegravir levels can be decreased by taking supplements or antacids containing aluminum, calcium, magnesium, or iron, or sucralfate, so take dolutegravir at least 2 hours before or 6 hours after these medications. Calcium and iron can be taken simultaneously with dolutegravir only if taken with food.

ACTIVIST MICHAEL BRODER:

I am on a Tivicay-containing regimen. Tivicay is safe, effective, and tolerable. There was 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-containing regimens. Your doctor can help you weigh the benefits against the risks.

Isentress HD (*and* Isentress)

raltegravir
RAL

INSTI **Integrase strand transfer inhibitor** ✔ Recommended as a component of initial regimen in certain clinical situations

GENERIC IS AVAILABLE

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 88 pounds (40 kg). Isentress is for adults and children weighing at least 4 pounds (2 kg). Both Isentress HD and Isentress can be taken without regard to food.

Isentress (but not Isentress HD) pediatric formulations are available as an oral suspension and flavored chewable tablets. Isentress dosing is based on weight for children less than 55 pounds; see package insert for dosing. The chewable tablets may be chewed or swallowed whole. Do not substitute chewable tablets or oral suspension for film-coated tablets.

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

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

POTENTIAL SIDE EFFECTS AND TOXICITY

In general, raltegravir is very well tolerated with infrequent side effects. Those reported in up to 3–4% of study 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: Biktarvy, Genvoya, Stribild, Tivicay, Triumeq, Dovato, Cabenuva, and Juluca. Isentress HD cannot be used with rifampin, but Isentress can; increase Isentress to 800 mg twice daily when using rifampin. Remember to decrease the raltegravir back to its original dose when you finish taking rifampin. There are no data on dosing of the chewable tablets with rifampin. There is no need to increase the raltegravir dose with rifabutin. With both Isentress HD and Isentress, avoid Gaviscon and other antacids containing aluminum or magnesium. Calcium-containing antacids such as Tums (calcium carbonate) can be used with Isentress, but not Isentress HD. Other acid reducers (such as Pepcid, Zantac, Prilosec, and Prevacid) are okay to use. Raltegravir is not recommended with carbamazepine or phenobarbital. Raltegravir can be used with Harvoni, Zepatier, or Epclusa. Unlike Isentress, Isentress HD cannot be used with Intelence or boosted Aptivus. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions not listed here.

MORE INFORMATION

Isentress HD was approved in 2017. While the original formulation, Isentress, was well tolerated and highly effective, its twice-daily dose was seen by some as a 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
isentress.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

DR. MELANIE THOMPSON:

Raltegravir, the oldest INSTI, was revolutionary at the time, but has been largely sidestepped in favor of the second-generation INSTIs. It is more susceptible to viral resistance than bictegravir, dolutegravir, or cabotegravir. It also requires twice-daily dosing or, in the HD formulation, two pills taken once daily, and it is not available as 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.

ACTIVIST MICHAEL BRODER:

Isentress, approved in 2007, was the first INSTI to enter clinical use. Isentress is one pill twice a day (original Isentress) or two pills once a day (Isentress HD). Isentress is currently recommended for initial therapy in certain situations, but not for most people starting treatment for the first time. To put it bluntly, Isentress is not as good, practically speaking, as the INSTIs dolutegravir (Tivicay) or bictegravir (a component of Biktarvy). For one thing, Isentress has a lower barrier to resistance than dolutegravir or bictegravir. In addition, Isentress-based regimens require more pills than other INSTI-based regimens. Moreover, Isentress is the only current INSTI that is not included as part of an STR. Given other available options, there are usually better alternatives to an Isentress-containing regimen. If your provider recommends an Isentress-containing regimen, they may have a good reason, but make sure they tell you what it is.

Prezista
darunavir
DRV

Prezcobix
darunavir/cobicistat
DRV/COBI

PI **Protease inhibitor**

PI/PKE Fixed-dose combination containing a **protease inhibitor and a pharmacokinetic enhancer** (booster)

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

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 with food for pregnant individuals and for people who have at least one Prezista-related resistance mutation. Prezista should always be taken with Norvir or Tybost. Suspension needs to be taken with Norvir or Tybost, with food. Suspension should be shaken before each use and stored at room temperature. Do not refrigerate.

PREZCOBIX: One tablet (800 mg of darunavir boosted by 150 mg cobicistat) once daily with food, in people with no darunavir-associated drug resistance, including both treatment-experienced and treatment-naïve 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 classes. 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 sulfa 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, lomitapide, lurasidone, naloxegol, pimozide, triazolam, oral midazolam, ranolazine, rifampin, Revatio, St. John's wort, or Zepatier. Do not use lovastatin or simvastatin, or co-formulations containing these drugs. Alternatives are atorvastatin and rosuvastatin (dose of either should not exceed 20 mg per day). Not recommended with avanafil, rifapentine, rivaroxaban, or salmeterol. Erectile dysfunction drugs should not exceed 10 mg Cialis or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours. Titration or decreased dose may be needed for buspirone, diazepam, estazolam, and zolpidem. Therapeutic drug monitoring is recommended for amiodarone, bepridil, disopyramide, flecainamide, systemic lidocaine, mexiletine, propafenone, and quinidine. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are many other drug interactions not listed here.

PREZISTA: Not recommended with everolimus, or ticagrelor, or with irinotecan. Monitoring of clonazepam, phenytoin, and phenobarbital is recommended. Tramadol dose decrease may be needed. Monitor therapeutic effects and adverse reactions with use of some analgesics, such as fentanyl and oxycodone. Reducing dose of rifabutin is recommended. Pitavastatin may be used with no dose adjustment, but pravastatin should be used with caution and started at the lowest dose possible. Monitor for increased side effects from these medications. Reduce clarithromycin dose by 50–75% in kidney impairment. Isavuconazole, posaconazole, ketoconazole, and itraconazole should be used with caution (maximum dose is 200 mg per day for ketoconazole and itraconazole). 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, betamethasone, dexamethasone, methylprednisolone, mometasone, and triamcinolone. Use alternative corticosteroid and monitor for signs of Cushing's syndrome. Beclomethasone, prednisolone, and prednisone as alternative corticosteroids may be considered, particularly for long-term use. Monitoring is recommended for co-administration with drospirenone due to the potential for hyperkalemia. Monitoring is recommended with buprenorphine, buprenorphine/naloxone, and methadone.

PREZCOBIX: Do not take with carbamazepine, dexamethasone, phenytoin, or phenobarbital, or with colchicine (in people with kidney or liver impairment). Not recommended to be taken with betamethasone, budesonide, ciclesonide, everolimus, fluticasone, Mavyret, methylprednisolone, mometasone, rifapentine, salmeterol, ticagrelor, triamcinolone, 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.

DR. MELANIE THOMPSON: Darunavir (Prezista) is the protease inhibitor backbone of Prezcobix as well as Symtuza. It has a high genetic barrier to resistance, meaning that a few missed doses are not likely to select for resistant viruses. But its Achilles heel is that it requires boosting with ritonavir or cobicistat. That is one of the key reasons that darunavir-based regimens are not recommended for initial therapy for most people with HIV. A large observational study found darunavir to be associated with higher cardiovascular risk than atazanavir. Cobicistat should not be given in pregnancy due to inadequate drug levels, so ritonavir should be used as a booster in this setting.

ACTIVIST MICHAEL BRODER: Given other available options, it's hard to imagine why any provider nowadays would recommend a boosted regimen.

MORE INFORMATION

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

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

PREZCOBIX AWP

$2,672.56/month

Reyataz

atazanavir sulfate
ATV

PI **Protease inhibitor**

Evotaz

atazanavir/cobicistat
ATV/COBI

PI/PKE Fixed-dose combination containing a **protease inhibitor and a pharmacokinetic enhancer (booster)**

✔ Recommended as components of initial regimen in certain clinical situations

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 Intelence or Sustiva is not recommended. Use in treatment-experienced people depends on protease inhibitor drug resistance. 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, abnormal 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 Viramune (nevirapine). Tybost is not interchangeable 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 chewable antacids, 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, herbals, 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 Epzicom 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. Voriconazole 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 carbamazepine, 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.

DR. MELANIE THOMPSON: Atazanavir has more toxicities and drug interactions than INSTIs and is not recommended for initial therapy in most people. Acid blockers can't be used with atazanavir, and the drug must be taken with food. Atazanavir-based regimens are not often used these days because of the high incidence of jaundice due to indirect hyperbilirubinemia (high bilirubin in the blood) and an increased risk of kidney and gallbladder stones, as well as kidney toxicity. On the bright side, large cohort studies have not found an association between atazanavir and cardiovascular disease. Unboosted atazanavir is FDA-approved for people who have not taken treatment before, but it is not recommended by DHHS or IAS-USA guidelines panels. Ritonavir should be used as a booster in pregnancy, with 400 mg atazanavir.

ACTIVIST MICHAEL BRODER: Atazanavir unboosted already has a pretty bad side effect profile, and boosting makes side effects worse. Given other available options, it's hard to imagine why any provider nowadays would recommend an atazanavir-containing regimen.

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

EVOTAZ AWP

$1,926.56/month

Norvir

ritonavir
RTV

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

GENERIC IS AVAILABLE

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

STANDARD DOSE

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

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

Approved for children older than one month with dosing based on body surface area; the use in children depends on the co-administered PI. Capsule formulation requires refrigeration, but tablet does not. Liquid formulation available (80 mg/mL) in peppermint caramel flavor, but is not very palatable. The taste of the liquid can be improved by mixing with chocolate milk, peanut butter, Ensure, or Advera within one hour of dosing. The liquid formulation should not be taken by individuals who 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.

POTENTIAL SIDE EFFECTS AND TOXICITY

The side effect potential of Norvir is much lower now that it is only used as a booster at low doses. Most common side effects include stomach pain, nausea, diarrhea, and vomiting. Other less common side effects may include fatigue; tingling/numbness around the mouth, hands, or feet; loss of appetite; and taste disturbances. Norvir can also increase cholesterol and triglyceride levels. Measure liver function before starting and then monitor, with perhaps closer monitoring for those with underlying liver problems, especially during the first several months. No dose adjustment necessary with mild to moderate liver disease, but Norvir is not recommended for those with severe liver impairment.

POTENTIAL DRUG INTERACTIONS

Norvir interacts with many drugs. Of note, Norvir is not interchangeable with Tybost. Also, Norvir tablets are not interchangeable with Norvir capsules. Do not take with alfuzosin, amiodarone, flecainide, lurasidone, propafenone, oral midazolam, triazolam, pimozide, ranolazine, Revatio, rifapentine, rifampin, voriconazole, ergot derivatives, or the herb St. John's wort. Do not use lovastatin or simvastatin or co-formulations containing these drugs (Advicor and Vytorin) for the treatment of high cholesterol. Cholesterol-lowering alternatives are atorvastatin, rosuvastatin, pravastatin, pitavastatin, and fluvastatin, but should be used with caution and started at the lowest dose possible; monitor for increased side effects. Norvir increases levels of nasal and inhaled fluticasone (found in Advair, Flonase, Breo Ellipta, Arnuity Ellipta, and Flovent), which may lead to Cushing's syndrome. Use an alternative corticosteroid and monitor for signs of Cushing's syndrome (increased abdominal fat, fatty hump between the shoulders, rounded face, red/purple stretch marks, bone loss, increased appetite, possible high blood pressure, and sometimes diabetes). Trazodone concentrations may increase; a lower dose of trazodone is recommended. Norvir may decrease levels of methadone, therefore titrate dose of methadone to clinical effect. Use caution with anticonvulsants such as carbamazepine, phenobarbital, and phenytoin. Use calcium channel blockers (amlodipine, nifedipine, and others) with caution. Norvir may alter warfarin levels; additional monitoring is required. Taking Norvir with most other blood thinners (anticoagulants), such as Xarelto, is not recommended; however, it can be used with apixaban (Eliquis) with monitoring and an adjusted dose of apixaban. Norvir can increase anticoagulant concentrations (and thereby increase risk of bleeding) or decrease their concentrations (and thereby decrease effectiveness). Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours. Monitor for increased side effects of these medications, such as visual disturbances, low blood pressure, dizziness, and prolonged painful erection lasting longer than four hours. Effectiveness of oral contraceptives may be decreased; consider using other or alternative methods of contraception. Levels of the street drug ecstasy are greatly increased by Norvir, and at least one death has been attributed to the combination. Using Norvir with methamphetamines can result in up to a 2–3-fold increase in methamphetamine concentrations, increasing the risk for overdose. GHB, another street drug, as well as cocaine are also dangerous with Norvir. Clarithromycin levels can increase by up to 80%. Co-administer bosentan, salmeterol, and immunosuppressants with caution. If co-administered, a lower dose of colchicine is recommended. Norvir, when combined with another PI, may be taken with Sovaldi, Daklinza (dose may need adjustment), Epclusa (monitor for tenofovir toxicity if TDF is part of regimen), and Harvoni (if TDF is not part of HIV regimen). Norvir + PI should not be taken with Olysio, Viekira Pak, or Zepatier. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are many other drug interactions that are not listed here.

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. Pharmacists, 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. Some liver toxicity also has been seen, and ritonavir raises triglyceride levels. 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 of 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 Norvir 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 what 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**

Tybost cobicistat COBI

PKE **Pharmacokinetic enhancer (booster)**

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

STANDARD DOSE

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

For adults and children weighing at least 77 pounds (if taken with atazanavir, brand name Reyataz) or at least 88 pounds (if taken with darunavir, brand name Prezista or in the single-tablet regimen Symtuza; 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, dihydroergotamine, dronedarone, ergotamine, irinotecan, simvastatin, lovastatin, lurasidone, methylergonovine, ranolazine, rifampin, pimozide, triazolam, oral midazolam, Revatio, or St. John's wort. Tybost may increase levels of nasal or inhaled fluticasone (Flonase, Advair, Breo Ellipta, Arnuity Ellipta, and Flovent). Use an alternative corticosteroid and monitor for signs of Cushing's syndrome (increased abdominal fat, fatty hump between the shoulders, rounded face, red/purple stretch marks, increased appetite, bone loss, possible high blood pressure, and sometimes diabetes). No significant interactions with beclomethasone. Tybost may increase levels of certain calcium channel blockers, beta blockers, HMG-CoA reductase inhibitors (statins or cholesterol medicines), anticoagulants, antiplatelets, antiarrhythmics, antidepressants, sedative-hypnotics, rifabutin, bosentan, erectile dysfunction agents, inhaled corticosteroids, and norgestimate. Caution should be taken, with possible dose adjustments of these medications, when used with Tybost. Sporonox (antifungal) and Biaxin (antibiotic) may increase Tybost concentrations. Tybost may also increase Biaxin levels. Rifabutin and some anti-seizure medications, such as carbamazepine (Tegretol), phenobarbital, and phenytoin (Dilantin) may decrease Tybost drug levels. Start metformin at lowest dose and titrate based on tolerability and clinical effect. Do not take with Olysio, Viekira Pak, or Zepatier. Avoid Harvoni if tenofovir disoproxil fumarate (TDF) is part of the HIV regimen. Tybost has similar drug interactions as Norvir, but they are not interchangeable, and there may be some drug interactions with Tybost that are not observed with Norvir. Tybost may increase levels of methamphetamines. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

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 hiv-druginteractions.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.

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.")

ACTIVIST 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 PIs and INSTIs. 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.

MORE INFORMATION

Tybost is not an HIV medication. It is used to boost blood levels of Prezista and Reyataz and is available in fixed-dose tablets with those medications (see Evotaz and Prezcobix, also the single-tablet regimen Symtuza). Cobicistat is also part of the single-tablet regimens Genvoya and Stribild to boost the elvitegravir component. All of these aforementioned regimens are recommended in the DHHS treatment guidelines for use in certain clinical situations. Tybost shares some of the same side effects, such as increased cholesterol and increased triglycerides, as Norvir; however, in clinical trials they were less pronounced. Tybost co-administered with elvitegravir, darunavir, or atazanavir should not be initiated in pregnant individuals and is not recommended during pregnancy. Inadequate levels of ART (antiretroviral therapy) in second and third trimesters as well as viral breakthroughs have been reported. Tybost is not recommended during pregnancy. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$321.02/month

Descovy

emtricitabine/tenofovir alafenamide
FTC/TAF

NRTI Fixed-dose combination of two nucleoside reverse transcriptase inhibitors (nucleoside, or "nuke")

★ Recommended as a component of initial regimen for most people

STANDARD DOSE

One tablet once daily, without regard to food. Tablet contains 200 mg emtricitabine and 25 mg tenofovir alafenamide (TAF). For adults and children weighing at least 55 pounds (25 kg), or 77 pounds (35 kg) if taking Descovy with a boosted protease inhibitor. Must be taken in combination with another antiretroviral(s) that does not contain the medications in this drug combination.

Take a missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. Descovy's prescribing information indicates that it should not be used if CrCl is less than 30 mL/min, but data have shown that it can be used safely in 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: "Postmarketing 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 Temixys, Emtriva, Epivir-HBV, Hepsera, Truvada, Viread, or Vemlidy (TAF), used for the treatment of hepatitis B. Use caution with drugs that negatively affect the kidneys, including chronic use or high doses of anti-inflammatory drugs for pain such as Advil or Motrin (ibuprofen) and Aleve (naproxen). Descovy should not be taken with certain anticonvulsants (including carbamazepine, oxcarbazepine, phenobarbital, and phenytoin), Aptivus/Norvir, rifabutin, rifampin, rifapentine, or St. John's wort. Can be used with hepatitis C drugs such as Epclusa, Harvoni, or Zepatier. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions 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 up to 90%. This results in a decreased impact on kidney and bone demineralization but maintains potent antiviral activity in the CD4 cell. In clinical trials, fewer kidney and bone issues were observed with TAF than with TDF, and significant improvements were observed when switching from TDF to TAF. The long-term impact of TAF on 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 for use in pregnancy, according to DHHS perinatal guidelines. Descovy tablets are relatively small compared to Truvada and other combination tablets, which may be helpful to people who have difficulty swallowing. Pregnant individuals can voluntarily enroll 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 Odefsey. 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.

Truvada

emtricitabine/tenofovir disoproxil fumarate
FTC/TDF

NRTI **Fixed-dose combination of two nucleoside reverse transcriptase inhibitors (nucleoside, or "nuke")**

★ Recommended as a component of initial regimen for most people

■ GENERIC IS AVAILABLE

■ 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) dosages: 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 elimination of 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, Hepsera, Vemlidy, or Viread, all used for the treatment of hepatitis B. Tenofovir DF decreases the concentration levels of Reyataz, therefore when Reyataz is taken with Truvada or Viread, it is recommended that Reyataz 300 mg be taken with Norvir 100 mg or Tybost 150 mg (all as a single daily dose with food). In addition, Reyataz/Norvir, Prezista/Norvir, and Kaletra increase tenofovir DF concentrations. It is recommended that people taking Reyataz/Norvir, Prezista/Norvir, or Kaletra with Truvada should be monitored for Truvada-associated adverse events, particularly decreases in kidney function. Avoid taking Truvada with drugs that negatively affect the kidneys, including chronic use or high doses of anti-inflammatory drugs for pain such as Advil or Motrin (ibuprofen) and Aleve (naproxen). Truvada may be used with hepatitis C drugs Harvoni or Zepatier, depending on the third drug in the HIV regimen; monitor for tenofovir toxicities if used with Epclusa. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions not listed here.

■ MORE INFORMATION

Don't believe the lawsuit advertisers: Truvada is a safe medication to take. As with any drug therapy, some people will experience side effects. Adverse events are rare and usually reversible. 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 apregistry.com.

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, side effects of highest concern include 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 disease or low bone density, 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, Stribild, 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 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 rather than Descovy, they may well have a good reason, but make sure they tell you what it is.

■ MANUFACTURER

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

■ AVERAGE WHOLESALE PRICE

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

Cimduo *and* Temixys

lamivudine/ tenofovir DF
3TC/TDF

NRTI 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 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 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 warranted upon discontinuation. Call your health care provider right away if you develop any of the following signs or symptoms of hepatitis: yellowing of the skin or whites of the eyes; dark or tea-colored urine; pale-colored bowel movements; nausea or vomiting; loss of appetite; or pain, aching, or tenderness on the right side below the ribs. Contains lactose, which can cause some abdominal discomfort, especially in people sensitive to lactose. Read weight discussion in the online version of this page.

POTENTIAL DRUG INTERACTIONS

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

MORE INFORMATION

Cimduo and Temixys are slightly different versions of Truvada, but contain 3TC instead of Truvada's FTC. The two meds are essentially equivalent. The niche for these medications is that they may be a cheaper option for some insurance plans because they contain generic drugs. They also allow for some new or unique co-formulations (such as with Delstrigo, Symfi, and Symfi Lo). 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: **$1,206.56**/month
Temixys: Not available on formulary used

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. Generic TDF now is combined with generic 3TC in Cimduo and Temixys, essentially the same drugs made by different 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 "knock-off"). Why do we need both Cimduo and Temixys? Medically, we don't. These are simply competing brands of more-or-less equivalent products, a little like Coke and Pepsi, or Nike and Reebok. Gilead's patent on emtricitabine expired last 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—but verify.

Epzicom

abacavir/lamivudine
ABC/3TC

NRTI Fixed-dose combination of **two nucleoside reverse transcriptase inhibitors** (nucleosides, or "nukes")

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

GENERIC IS AVAILABLE

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, alternative doses may be obtained by using the individual components of this medication as needed.

➤ SEE THE INDIVIDUAL DRUGS CONTAINED IN EPZICOM: Epivir and Ziagen.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Common side effects may include headache, nausea, fatigue, depressed mood, dizziness, diarrhea, rash, or insomnia. Of note is the hypersensitivity reaction (HSR, an allergic-like reaction) warning on abacavir (see Ziagen for details of symptoms). To minimize the risk for HSR, a simple blood test for HLA-B*5701 (a genetic marker) should be done before starting an HIV regimen containing abacavir to identify people at higher risk for this reaction. A negative HLA-B*5701 test does not mean you won't have 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 large observational studies suggest abacavir may increase the risk of cardiovascular events, including myocardial infarction (MI, or heart attack), in people with risk factors such as smoking, diabetes, uncontrolled high blood pressure, older age, high cholesterol, family history of heart disease, and drug use. Other studies have found no increased risk. To date, no absolute consensus has been reached on the association 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; nausea or vomiting; loss of appetite; or pain, aching, or tenderness on the right side below the ribs.

POTENTIAL DRUG INTERACTIONS

See the individual drugs contained in Epzicom—Epivir and Ziagen. It is important to take Epzicom only with other HIV medications recommended by your provider because Epzicom and its equivalent drugs are contained in other HIV medications: Atripla, Biktarvy, Cimduo, Combivir, Complera, Delstrigo, Descovy, Dovato, Emtriva, Epivir, Genvoya, Odefsey, Stribild, Symfi, Symfi Lo, Symtuza, Temixys, Triumeq, Trizivir, Truvada, or Ziagen; also, Epivir-HBV 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, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions not listed here.

MORE INFORMATION

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

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

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

DR. MELANIE THOMPSON:

Abacavir/3TC is generic and ViiV will discontinue brand name Epzicom tablets as of January 1, 2024. The main drawback for this combo is the need for screening to avoid abacavir hypersensitivity before beginning the drug (see Ziagen). Also, when used with efavirenz or atazanavir + ritonavir, viral load should be 100,000 copies/mL or below.

In early clinical trials, the most common side effects with abacavir were nausea, headache, malaise and fatigue, vomiting, and dreams/sleep disorders.

Observational studies have found conflicting evidence on whether abacavir is associated with cardiovascular disease. The FDA concludes that the evidence is "inconclusive." DHHS guidelines recommend avoiding abacavir in persons with, or at high risk for, cardiovascular disease.

ACTIVIST MICHAEL BRODER:

Epzicom (approved in 2004) is a fixed-dose combination (FDC) of two NRTIs—Epivir (lamivudine) and Ziagen (abacavir). Epzicom is recommended for most people starting therapy for the first time in combination with the INSTI Tivicay (dolutegravir). Epzicom cannot be taken by people with a certain gene that makes them susceptible to a life-threatening allergic reaction to abacavir (your doctor will test you for the gene before prescribing Epzicom). Epzicom should not be taken by people with hepatitis B virus (HBV). Some studies have found increased rates of heart disease among people taking the abacavir component of Epzicom. Both components of Epzicom share a resistance mutation (called M184V); so, while the Epzicom "backbone" is recommended for most people starting treatment for the first time, folks who have previously been on a regimen that contained Epivir (lamivudine), Ziagen (abacavir), or Emtriva (emtricitabine) should make sure their provider is aware of their treatment history.

Emtriva

emtricitabine
FTC

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

★ Recommended as a component of initial regimen for most people

GENERIC IS AVAILABLE

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) (cotton candy flavored) 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.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Emtriva is very well tolerated. The most common side effects (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 Epclusa, Harvoni, or Zepatier, depending on the other components in the HIV regimen. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not.

MORE INFORMATION

This drug is used almost exclusively as 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, Stribild, and Symtuza). Sometimes, drug resistance that the virus develops against emtricitabine makes the virus reproduce at a slower rate. This drug resistance can also improve the antiviral activity of Retrovir (zidovudine, or AZT—very rarely taken today) and Viread or Vemlidy (tenofovir), and for that reason, some providers continue Emtriva treatment in combination with other antiretrovirals after resistance develops. 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 apregistry.com.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

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

DR. MELANIE THOMPSON:

Emtricitabine, 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 3TC and is regarded as interchangeable with 3TC 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, Stribild, 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.

Epivir lamivudine 3TC

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

★ Recommended as a component of initial regimen for most people

GENERIC IS AVAILABLE

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 for weight-based dosing.

Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. The 150 mg tablets are scored and may be split. Based on drug properties, tablets may be crushed and added to a small amount of semi-solid food or liquid for immediate consumption. Epivir is also available as an oral solution (10 mg/mL) (strawberry-banana flavor) for children and adults who are not able to swallow the tablets. 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: yellowing of the skin or whites of the eyes; dark or tea-colored urine; pale-colored bowel movements; nausea or vomiting; loss of appetite; or pain, aching, or tenderness on the right side below the ribs.

POTENTIAL DRUG INTERACTIONS

Do not take with Cimduo or Temixys, Descovy, Emtriva, Epivir-HBV, Hepsera, or Truvada, which are used for the treatment of hepatitis B. No other significant drug interactions. Epivir may be used with hepatitis C drugs Epclusa, Harvoni, or Zepatier, depending on the other components in the HIV regimen. Avoid use of sorbitol-containing medicines with lamivudine; there are many, such as acetaminophen liquid (Tylenol liquid and others). Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not.

MORE INFORMATION

This drug is used almost exclusively as part of combination tablets. Epivir (lamivudine) is similar to Emtriva (emtricitabine): both treat HIV and HBV and have the same resistance profile, meaning that if your virus is resistant to one drug, it will be resistant to the other. If your HIV develops resistance to lamivudine, it doesn't mean that your HBV is also resistant to it. Sometimes, drug resistance that the virus develops against lamivudine makes the virus reproduce at a slower rate. This drug resistance can also improve the antiviral activity of Retrovir (zidovudine, or AZT—very rarely taken today) and Viread or Vemlidy (tenofovir), and for that reason, some providers continue Epivir treatment in combination with other antiretrovirals after resistance develops. Lamivudine is also available in several combination products: Cimduo and Temixys (with tenofovir DF), Combivir (with zidovudine), Epzicom (with abacavir), Trizivir (with zidovudine and abacavir), Symfi and Symfi Lo (with tenofovir DF and efavirenz), Delstrigo (with tenofovir DF and doravirine), Dovato (with dolutegravir), and Triumeq (with dolutegravir and abacavir). 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 component 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; GO TO apregistry.com.

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

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 (FDCs) 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

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

★ Recommended as a component of initial regimen for most people

GENERIC IS AVAILABLE

STANDARD DOSE

One 300 mg tablet once daily, without regard to food. Must be taken in combination with another antiretroviral(s).

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. Decreases in bone mineral density (BMD) have been observed. BMD monitoring should be considered for people who have a history of bone fracture due to bone disease or are at risk for osteopenia or osteoporosis. 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. Viread may cause kidney toxicities. Creatinine clearance (CrCl) should be assessed before initiating treatment. In addition to CrCl, glucose and protein in the urine and serum phosphorus should be monitored more often in people at risk for kidney problems. Tell your provider about any pain in extremities, persistent or worsening bone pain and fractures, with or without muscular pain or weakness, as well as any concerning changes in urinary habits, as these could be signs of bone or kidney problems. Prior to initiation, people should be tested for hepatitis B virus (HBV) infection. Severe exacerbations of hepatitis B have been reported in people co-infected with HBV 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; 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. 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 Vemlidy, all used for the treatment of hepatitis B. Viread decreases levels of Reyataz; therefore, Reyataz 300 mg must be boosted with Norvir 100 mg or Tybost 150 mg (taken together with food) when used in combination with TDF. Kaletra, Prezista/Norvir, and Reyataz/Norvir increase Viread levels, but there is no dose adjustment needed. 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, herbals, and supplements you are taking or thinking of taking, prescribed or not.

MORE INFORMATION

TDF with emtricitabine (as Truvada) and TDF with lamivudine (as Cimduo or Temixys) are 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 Stribild. 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 3TC. 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 ViiV 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.

Ziagen abacavir ABC

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

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

GENERIC IS AVAILABLE

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 dreams/sleep disorders. In pediatric people, 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 ache, chills, diarrhea, vomiting, abdominal pain, respiratory symptoms (cough, difficulty breathing, sore throat), and/or joint pain. Symptoms are listed on the patient information sheet and warning card that you receive each time you fill your prescription. You should keep the warning card with you. HSR might be confused with flu, but symptoms of HSR usually worsen, very slowly, and with every dose.

People who think they are experiencing HSR must be evaluated by an experienced HIV provider right away before they stop taking abacavir. Do not use a skin patch test to confirm HSR. Symptoms usually resolve after permanent discontinuation. If you develop HSR, abacavir should be stopped and you can never take abacavir or any product containing abacavir (Epzicom, Ziagen, or Triumeq) again (starting again is called *rechallenging*). Rechallenging can cause a rare life-threatening reaction. This does not apply to a missed dose when there is no HSR, but talk with your healthcare provider and watch for symptoms if you've stopped the drug for a few days, preferably under the observation of others who can call for medical help if you develop symptoms. An HSR can technically occur at any time, regardless of how long you have been taking the medication; however, it is much more likely to occur when you start (or re-start) the medication (90% occur within the first 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, high cholesterol, 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. People who are at high risk for heart disease should discuss risks with their provider and they should be monitored more closely.

POTENTIAL DRUG INTERACTIONS

Alcohol can increase abacavir levels and therefore can increase the possibility of side effects.

MORE INFORMATION

The ACTG A5202 study found that abacavir/lamivudine (Epzicom) was inferior to tenofovir/emtricitabine (Truvada) in getting people undetectable when their pre-treatment viral load was over 100,000 copies/mL. However, when combined with Tivicay (dolutegravir), Epzicom performed just as well as Truvada in people with high viral loads (over 100,000 copies/mL). Hence, Triumeq is the only abacavir-containing regimen recommended by DHHS as initial therapy for most HLA-B*5701-negative people. It is recommended 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 "Alternative" list last year for this population. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com
(877) 844-8872

AVERAGE WHOLESALE PRICE

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

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 ever had abacavir hypersensitivity, you should never take abacavir again, and be sure your medical chart is marked for "allergy" to abacavir.

Abacavir continues to be useful for people who can't take TDF because of kidney problems or osteopenia/osteoporosis. 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 an NRTI that is recommended for most people starting ART for the first time in combination with the NRTI Epivir (lamivudine) and the INSTI Tivicay (dolutegravir), as Triumeq. Ziagen cannot be taken by people who have a certain gene that makes them more likely to have a life-threatening allergic reaction to abacavir (your doctor will test you for the gene before prescribing Ziagen). Some studies have found increased rates of heart disease among people on Ziagen. 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.

Edurant rilpivirine RPV

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

✔ Recommended as a component of an initial regimen in certain clinical situations in combination with Descovy or Truvada (as Odefsey or Complera)

STANDARD DOSE

One 25 mg tablet once daily with a standard meal. For adults and children (12 years of age and older weighing at least 77 pounds, or 35 kg) taking HIV treatment for the first time (treatment-naïve) 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/mm^3 before starting Edurant due to higher rates of virologic failure in these people. The CD4 requirement, however, is no longer on the drug label.

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

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

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Edurant is a very tolerable medication. Moderate to severe side effects are uncommon. Most common side effects occurring in 3–5% of study subjects were insomnia, headache, rash, and depressive disorders. Stop taking Edurant and see a medical provider right away if allergic reaction or rash occurs with any of the following: fever, trouble breathing or swallowing, blisters, mouth sores, redness or swelling of the eyes, or swelling of the face, lips, mouth, tongue, or throat. Tell your doctor right away if you experience feelings of sadness, hopelessness, anxiety or restlessness, or have suicidal thoughts or actions. A small study showed a higher rate of depressive disorders in adolescents (19.4%—seven out of 36 youths—vs. 9% for adults), which may or may not have been related to Edurant. Edurant also has minimal negative effects on LDL ("bad") cholesterol, total cholesterol, and triglycerides compared to Sustiva. Edurant improved HDL ("good") cholesterol slightly less than Sustiva. Liver problems can occur, but are very rare. The risk may be greater for people with a history of hepatitis B or C, but may occur in people without a history of liver disease. Edurant can cause 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 antiseizure medications carbamazepine, oxcarbazepine, phenobarbital, or phenytoin; the anti-TB drugs rifampin and rifapentine; proton pump inhibitors (Aciphex, Dexilant, Nexium, Prevacid, Protonix, and Prilosec); or St. John's wort. Do not take with more than one dose of the injectable steroid dexamethasone (sometimes given in the ER or hospital). Antacids or other products containing aluminum, calcium carbonate, or magnesium hydroxide should be taken two hours before or at least four hours after Edurant. Acid-reducing drugs (Pepcid, Tagamet, Zantac, and Axid) should be taken 12 hours before or four hours after an Edurant dose. If administered with rifabutin, the dose of Edurant should be increased to two 25 mg tablets once daily with a meal. When rifabutin is stopped, Edurant dose should be decreased to 25 mg daily. Monitor for worsening of any fungal infections when Edurant is used with antifungal medications such as fluconazole, itraconazole, ketoconazole, posaconazole, and voriconazole; dose adjustment for these medications may be needed. Use azithromycin when possible instead of clarithromycin, erythromycin, and telithromycin. Methadone levels are reduced slightly and people should be monitored for symptoms of withdrawal. Edurant should be used with caution when taken with other medications with a known risk for torsades de pointes or QT prolongation (these abnormal heart rhythms can make the heart stop).

DR. MELANIE THOMPSON:

Oral rilpivirine is primarily used as a component of the STRs Odefsey, Complera, and Juluca. It should only be used when viral load is below 100,000 copies/mL and CD4 is at least 200 cells/mm^3. Rilpivirine can be associated with depression or headache, liver toxicity (especially in people with hepatitis B or C), and rash, including a severe hypersensitivity reaction. Other side effects include risk of kidney stones or gallstones. There are many important drug-drug interactions with rilpivirine. For example, it should not be taken with antacids or acid blockers, or proton-pump inhibitors such as Prilosec or Pepcid, as acid is required for absorption. It can lower the levels of other drugs, such as methodone, and rilpivirine levels are decreased by some seizure and tuberculosis medicines, dexamethasone, and St. John's wort. There are other drug interactions also, so it's a good idea to discuss any drugs you take, including over-the-counter meds, with your HIV care provider. Rilpivirine should be taken with a meal of at least 390 calories for best absorption.

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 must be taken with food (at least 400 calories). Edurant has significant drug-drug interactions with antiseizure medications, anti-TB drugs, and a type of antacids called proton pump inhibitors, among others. A long-acting injectable formulation of rilpivirine is included in Cabenuva (alongside the long-acting INSTI cabotegravir) and is approved for "stable switches" (that is, by people undetectable on another regimen for at least six months). Given 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.

MORE INFORMATION

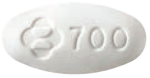
Rilpivirine combined with dolutegravir was approved by the FDA in late 2017; see Juluca. A long-acting injectable formulation of rilpivirine was approved in 2021 along with a long-acting injectable formulation of cabotegravir to form a complete regimen given once a month or once every two months; see Cabenuva. Edurant is not DHHS recommended for treatment-naïve people with a pre-treatment viral load greater than 100,000 copies/mL and CD4 T cell count below 200 cells/mm^3. The CD4 requirement, however, is no longer on the drug label. A rilpivirine-based regimen may be advantageous for people with high risk for heart disease due to its relatively low impact on lipid profile. The clinical benefit of these findings has not been demonstrated. While its tolerability and safety profiles are advantages for Edurant, the greater potential for virologic failure in 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 background are insufficient to recommend at this time. For individuals with HIV-2, commonly found in some other countries, an NNRTI would not be recommended as HIV-2 is inherently resistant to NNRTIs. Edurant can be used during pregnancy, and is listed as a DHHS alternative NNRTI to use during pregnancy in combination with a two-NRTI backbone. According to the FDA, lower exposures of rilpivirine were observed during pregnancy; therefore, viral load should be monitored closely. 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



Pifeltro doravirine DOR

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

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Most common side effects (with an incidence of 5% or greater) observed in Pifeltro studies were nausea (7%), headache (6%), fatigue (6%), diarrhea (6%), and abdominal pain (5%). Rash, which is a common side effect of the 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.

POTENTIAL 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, phenobarbital, and phenytoin; the androgen receptor inhibitor enzalutamide; the antimycobacterials rifampin and rifapentine; the cytotoxic agent (cancer drug) mitotane; and the herbal St. John's wort. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions 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 standalone Pifeltro allows people to take it with the newer tenofovir alafenamide (TAF), found in Descovy, which has potentially less long-term renal and bone toxicity. On the other hand, TAF is associated with weight gain. Of course, the use of Pifeltro means the necessity for an extra pill, such as Descovy, or maybe more than one extra pill, depending on the regimen being used. Pifeltro was found to be non-inferior to boosted darunavir (Prezista) as well as efavirenz (Sustiva), with data now out to 96 weeks (2 years). Doravirine was superior to boosted darunavir at week 96 in terms of virologic suppression, but it should be noted there was a higher rate of study discontinuation in the boosted darunavir group. Doravirine is a non-nucleoside medication, and it should be noted that this drug class typically has a lower barrier to resistance, as well as extensive cross-resistance. Additionally, the emergence of resistance at the time of virologic failure has been reported with doravirine. Doravirine has tolerability advantages over efavirenz and has relatively favorable lipid effects when compared to both boosted darunavir and efavirenz. It also has fewer potential drug interactions than efavirenz or rilpivirine, and, unlike rilpivirine, virologic efficacy is not compromised among people with high baseline viral loads or low CD4 counts. Doravirine has not yet been directly compared to integrase inhibitor-based regimens in clinical trials. In 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]." For individuals with HIV-2, commonly found in some other countries, an NNRTI would not be recommended as HIV-2 is inherently resistant to NNRTIs. No adequate human data are available yet to establish whether or not Pifeltro poses a risk to pregnancy outcomes. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

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.

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.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$1,916.64/month

Sustiva

efavirenz
EFV

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

GENERIC 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.

POTENTIAL SIDE EFFECTS AND TOXICITY

Central nervous system (CNS) side effects (dizziness, insomnia, impaired concentration, abnormal or vivid dreams, and hallucinations) are most common at the start of treatment and usually diminish in two to four weeks. Bedtime dosing on an empty stomach can help reduce symptoms. Less common psychiatric symptoms (catatonia, depression, suicidal thoughts or actions, aggression, paranoid/manic reactions) may also occur. A 2014 study reviewed four previously published AIDS Clinical Trials Group (ACTG) studies regarding efavirenz and suicidal ideation and re-emphasized efavirenz has an association with suicidality (reported suicidal ideation or attempted or completed suicide), and should be used with caution in 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 raise levels of triglycerides (fat in the blood) and cholesterol. Efavirenz can cause a false positive for marijuana on certain drug tests. A more specific confirmatory test can be done. A link to birth defects in humans was not supported by meta-analyses. Individuals in their first trimester of pregnancy are recommended to continue taking efavirenz as long as their viral load remains undetectable; however, efavirenz should only be used if the potential benefit outweighs the potential risk, as when other treatment options are not available. Because of the association with suicidality and neuropsychiatric effects, it is also recommended to screen for antenatal and postpartum depression in women with HIV who are taking a regimen containing efavirenz. Regular monitoring for increased liver enzyme levels is recommended initially and during treatment for people with hepatitis B/C or liver disease.

POTENTIAL DRUG INTERACTIONS

Do not take with midazolam, pimozide, ergot derivatives, St. John's wort, or triazolam. May affect warfarin levels. Can decrease levels of buprenorphine and methadone—monitor for withdrawal. Increase Kaletra to two 200/50 mg tablets plus one 100/25 mg tablet twice daily (total 500/125 mg twice daily) (or 520/130 mg twice daily for oral solution) with food when taken with Sustiva. Kaletra cannot be taken once daily with Sustiva. When taken with Tivicay, increase the Tivicay dose to 50 mg twice daily. Treatment-experienced people should not take Reyataz with Sustiva, but for treatment-naïve people, Reyataz once-daily dose should be 400 mg boosted with Norvir. Increase Selzentry to 600 mg twice daily. Increase the Sustiva dose to 800 mg once daily with rifampin for people weighing 110 pounds (50 kg) or more. Rifabutin can be used as an alternative, but dose adjustment is needed. Should not be used with abacavir and lamivudine in 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, phenobarbital, or phenytoin, periodic monitoring of anticonvulsant and Sustiva levels should be done or alternative antiseizure drugs, such as levetiracetam, should be considered. May decrease effectiveness of birth control pills; consider the use of other contraceptives. Closer monitoring and dose adjustments may be required with posaconazole (avoid unless benefit outweighs potential risk) and itraconazole. The dose of voriconazole should be increased to 400 mg every 12 hours and the Sustiva dose should be decreased to 300 mg once daily using capsules; tablets should not be broken. Monitor effectiveness of clarithromycin or consider using azithromycin instead. Levels of immunosuppressants should be monitored when starting or stopping Sustiva. Cardizem, Lipitor, Pravachol, and Zocor doses may need to be adjusted. Titrate dose of bupropion and sertraline based on clinical response. Should not be taken with other medications that prolong QT interval or medications with a known risk for torsades de pointes. No dose adjustment with Harvoni. Don't take with Epclusa or Zepatier. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions 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 in African Americans. In pediatric HIV guidelines, Sustiva was downgraded in 2017 from "preferred" to an "alternative" component of an initial regimen for children ages 3–12 years. For individuals with HIV-2, commonly found in some other countries, an NNRTI would not be recommended as HIV-2 is inherently resistant to NNRTIs. Efavirenz is found in the single-tablet regimens Atripla, Symfi, and Symfi Lo (see those pages).

DR. 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.

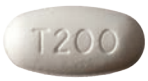
ACTIVIST MICHAEL BRODER: Sustiva breathed new life into the NNRTI class when it was on life support in the wake of bad pharmacology (delavirdine) and bad marketing (nevirapine). But it causes serious neurologic side effects such as nightmares, depression, and suicidal ideation that can make it difficult 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.

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



Intelence etravirine ETR

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

✔ For treatment-experienced people

GENERIC IS AVAILABLE

STANDARD DOSE

One 200 mg tablet, twice daily with a meal. Taking Intelence without food could result in a 50% decrease in the drug absorption and may lead to HIV drug resistance. Approved for treatment-experienced adults and children 2 years and older weighing at least 22 pounds (10 kg). See the package insert for specific weight-based dosing in children. Also available in 25 mg and 100 mg tablets. Must be taken in combination with another antiretroviral(s) that do not contain medication from the same drug class.

Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. People unable to swallow pills (Intelence tablets are "chalky") can dissolve tablets in one teaspoon (5 mL) of water or at least enough liquid to cover the medication; stir well until the water turns milky, add more water if desired—or use a small amount (about one tablespoon) of orange juice or milk as an alternative, always placing tablets in water first. Avoid warm (over 104° F) or carbonated beverages. Drink immediately, rinse the glass several times with water, orange juice, or milk, and completely swallow the rinse each time to make sure the entire dose is taken.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Generally well tolerated, but most common side effects of moderate to severe intensity in adults include rash as well as numbness, tingling, or pain in the hands or feet. Discontinue Intelence immediately if signs or symptoms of severe skin reactions or hypersensitivity reactions develop (including, but not limited to, severe rash or rash accompanied by fever, general malaise [general ill feeling], fatigue, muscle or joint aches, blisters, oral lesions, conjunctivitis, facial edema, hepatitis, eosinophilia, or angioedema). Levels of liver enzymes called transaminases should be monitored. Rash is associated with all of the current NNRTIs, but if you develop a rash from Intelence, you may still be able to take one of the other NNRTIs. In pediatric patients age 2 to 18, the frequency, type, and severity of adverse drug reactions were 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 rash of any grade, whereas rash of moderate intensity or greater was reported in 10% of adults. Rash is typically described as mild to moderate, pruritic (itchy), with pimple-like skin eruptions. For pediatric patients, rash usually appeared in the second week of therapy and generally resolved within a week. Discuss discontinuing etravirine if fever, blistering, or severe reaction occurs.

POTENTIAL DRUG INTERACTIONS

If Intelence is taken in combination with a protease inhibitor, the PI must be boosted with low-dose Norvir. Intelence should be avoided with Tivicay unless administered with one of the following combinations: Reyataz/Norvir, Prezista/Norvir, or Kaletra. Taking it in combination with Selzentry requires a Selzentry dose adjustment to 600 mg twice daily when used without a boosted PI, and 150 mg twice daily when used with a boosted PI. Do not take Intelence with Tegretol, Luminal, Dilantin, Priftin, Rifadin, or the herb St. John's wort. Use with caution when combined with the antifungals Diflucan and Vfend. Dose adjustments of the antifungals ketoconazole, itraconazole, and posaconazole may be needed. Dose adjustments of certain cholesterol medications may be needed based on clinical response, including Lipitor, Lescol, Mevacor, Livalo, and Zocor. Monitor the effectiveness of Coumadin (warfarin) and adjust dose as needed based on clinical response. Alternatives to Plavix should be considered when used with Intelence. Alternatives to clarithromycin—such as azithromycin—should be considered for treatment of MAC. Lower Valium dose may be needed. Use caution with systemic dexamethasone or consider alternatives. Intelence can be taken with rifabutin (Mycobutin) 300 mg daily; however, it should be avoided by people who are also taking a boosted PI. Concentrations of some antiarrhythmics may be decreased when co-administered with Intelence. Intelence and antiarrhythmics should be co-administered with caution. Drug concentration monitoring is recommended, if available. Intelence can be safely combined with methadone or buprenorphine with additional monitoring for potential signs of withdrawal. Intelence can also be safely combined with Viagra, Cialis, and Levitra, though a dosage adjustment of Viagra may be necessary. Interaction with Harvoni has not been studied, but based on the metabolism, a clinically significant interaction is not expected. Taking with Zepatier is not recommended. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

For people who have had virologic failure on an NNRTI-containing regimen, do not use Intelence in combination with a nucleoside backbone alone. Although taking once daily is not FDA approved, some providers are prescribing Intelence once daily (two of the 200 mg tablets) based on clinical trials that showed that once-daily Intelence was not inferior to Sustiva-based regimens. In Europe, it is approved as a once-daily medication. Once-daily dosing may improve patient adherence. Although the DHHS recommendation for Intelence specifies drug resistance strains before taking it, the drug label does not—you do not need to have drug resistance before taking Intelence. The TRIO study reported the combination of Intelence with Prezista/Norvir and Isentress in highly treatment-experienced people was successful in getting many people to undetectable. 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-naïve people who are pregnant. Individuals who become pregnant while taking etravirine may continue taking Intelence if viral suppression is effective and the regimen is well tolerated. The pharmacokinetics (PK) of etravirine are not significantly altered during pregnancy, and no dosage adjustment is necessary. The PK data demonstrated that exposure to total etravirine was generally higher during pregnancy compared with postpartum 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 voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

DR. MELANIE THOMPSON:

Etravirine was approved near the time of raltegravir and darunavir, and the three drugs together became an important nuke-free regimen for many people with virus that was resistant to NRTIs, older PIs, and efavirenz. It was never approved for initial therapy and it has largely been superceded by rilpivirine and doravirine, both of which can be given once daily with lower pill burden and fewer drug interactions.

ACTIVIST MICHAEL BRODER:

Intelence (etravirine, approved in 2008) is an NNRTI that is approved for use only in highly treatment-experienced people, meaning those who have already been on treatment for some time. Intelence is taken twice a day and must be taken with food. Intelence has problematic drug interactions with many widely prescribed drugs, including other HIV drugs. Given other available options, Intelence is not an obvious first choice for most people nowadays. If your provider recommends Intelence, they may have a good reason, but make sure they tell you what it is.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

100 mg, 120 tablets:
$1,693.80/month
Ietravirine generic:
100 mg, 120 tablets:
$1,609.11/month
Intelence: 200 mg, 60 tablets:
$1,693.80/month
etravirine generic:
200 mg, 60 tablets:
$1,609.11/month

Selzentry

maraviroc
MVC

EI **Entry/Attachment inhibitor:** CCR5 antagonist

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

■ GENERIC IS AVAILABLE

■ STANDARD DOSE

The recommended dose varies depending on other medications being taken but will be either 150, 300, or 600 mg twice daily (available in 150 mg and 300 mg tablets). Can be taken without regard to food. Approved for adults and children weighing at least 4.4 pounds (2 kg) and having a creatinine clearance of at least 30 mL/min (measurement of kidney function); dose depends on weight. Available in a 20 mg/mL oral solution as well as 25 mg and 75 mg tablets. Selzentry for children is dosed based on body weight. See the package insert or DHHS guidelines for weight-based dosing. The oral solution should be administered using the included press-in bottle adapter and oral dosing syringe. Must be taken in combination with another antiretroviral(s).

Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. Before starting Selzentry, a specific blood test called a Trofile is required to determine if this medication will work.

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

■ POTENTIAL SIDE EFFECTS AND TOXICITY

The most common side effects occurring in greater than 8% of studied 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, Stribild, Genvoya, Tybost, clarithromycin, and itraconazole; 300 mg twice daily if taken with Viramune, Isentress, Tivicay, Triumeq, Fuzeon, and all of the NRTIs and medications that do not affect the levels of Selzentry; and 600 mg twice daily if taken with medications that decrease levels of Selzentry, such as Atripla, Sustiva, Intelence, rifampin, and some anticonvulsants such as carbamazepine (Tegretol), phenobarbital, and phenytoin (Dilantin). Likely dose with rifapentine is 600 mg twice daily, but use with caution. Not recommended with St. John's wort. Selzentry may be co-administered with the hepatitis C medication Harvoni at a dose of 300 mg twice daily; however, ledipasvir (in Harvoni) may have potential to increase Selzentry levels. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

■ MORE INFORMATION

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

Selzentry is generally recommended only when HIV medications from other classes cannot be used or when a new class of medication is needed to construct a complete and durable treatment regimen for people who have drug resistance. Complex dosing, the need for a tropism test, and competition from newer drugs have dimmed some of the initial enthusiasm for this drug. In research bringing Trogarzo to market, Selzentry was often chosen to help create an optimized background regimen. Research participants had extensive HIV drug resistance. A tropism assay (Trofile, Trofile DNA, or HIV-1 Coreceptor Tropism with Reflex to UDS) is needed to determine if this medication will work. Results of a phenotypic tropism test (Trofile or Trofile DNA) may take up to a month to complete. Genotypic tests are also available and may provide a faster and less expensive alternative. Learn about Selzentry's mechanism of action at youtube.com/watch?v=oneYI0fhGa0. Selzentry only works for people with CCR5-tropic virus. Viral tropism refers to the types of HIV that a person can have, CCR5 (R5), CXCR4 (X4), or Dual-Mix Tropic (R5 and X4). Selzentry blocks CCR5, a 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. ViiV may cover the payment for the Trofile test under certain circumstances.

Selzentry seems to have minimal impact on lipid levels. DHHS guidelines do not recommend the use of maraviroc for treatment-naïve 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 the effects on a fetus. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

■ MANUFACTURER

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

DR. MELANIE THOMPSON: The only approved CCR5 inhibitor entry inhibitor, Selzentry is not for initial therapy. It can be helpful, however, for people who have substantial viral resistance and struggle to put together a viable regimen. The catch is that the virus must use the CCR5 receptor and this must be determined by use of a viral tropism test. Selzentry does not work if the virus uses the CXCR4 receptor or a mixture of the two, which is often the case with advanced HIV infection. The drug requires twice-daily dosing, making adherence more challenging, and drug-drug interactions may require dose adjustments. ViiV has announced that the 25 mg and 75 mg tablets of Selzentry will be discontinued as of January 1, 2024.

ACTIVIST MICHAEL BRODER: Selzentry (maraviroc, approved in 2007) is a chemokine co-receptor 5 (CCR5) antagonist. Selzentry 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. Selzentry is one pill twice daily with or without food. Given other available options, it's hard to imagine why any provider nowadays would recommend Selzentry, even for people who are highly treatment-experienced and have limited treatment options. If your provider recommends Selzentry, they may have a good reason, but make sure they tell you what it is.

■ AVERAGE WHOLESALE PRICE

150 mg, 60 tablets:
$1,959.70/month
300 mg, 60 tablets:
$1,959.70/month
generic: price not available at press time

Trogarzo ibalizumab-uiyk IBA

EI **Long-acting entry inhibitor:** CD4-directed post-attachment inhibitor

▼ For heavily treatment-experienced people

STANDARD DOSE

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

The first infusion takes at least 30 minutes. If no infusion-related adverse events occur, subsequent infusions take 15 minutes. Doses may be administered every two weeks at an inpatient and/or outpatient setting, including at-home infusion, if desired. All patients should be observed for 1 hour after completing first infusion. If no infusion-associated adverse reaction is noted, the post-infusion observation time can be reduced to 15 minutes 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.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

The most common adverse reactions observed in clinical studies were diarrhea (8%), dizziness (8%), nausea (5%), and rash (5%). Select lab abnormalities noted to occur in at least 5% of studied patients were increased bilirubin by greater than 2.6 times ULN (upper limit of normal), 5%; increased creatinine (greater than 1.8 times ULN or 1.5x baseline), 10%; increased lipase (greater than 3 times ULN), 5%; decreased leukocytes, 5%; and decreased neutrophils, 5%. Most (90%) of the adverse reactions reported were mild or moderate in severity. No formal studies were conducted to examine the effects of either renal or hepatic impairment on the pharmacokinetics of Trogarzo. Renal impairment is not anticipated to affect the pharmacokinetics of Trogarzo. 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 inside the womb. See Section 8.1 (Pregnancy) in the prescribing information for more details.

POTENTIAL DRUG INTERACTIONS

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

MORE INFORMATION

Essentially, this drug is for heavily treatment-experienced people with 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 viral load] may 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 is neither metabolized in the liver nor eliminated by the kidneys. Monoclonal antibodies such as ibalizumab are transported across the placenta as pregnancy progresses; therefore, the developing fetus has the potential to be exposed to Trogarzo. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

DR. MELANIE THOMPSON: Ibalizumab is an entry inhibitor that has activity 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, and 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 of the financial burden. 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 a 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 any eligible 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)

Rukobia

fostemsavir
FTR

AI **Entry/attachment inhibitor:** GP120 attachment inhibitor

▼ For heavily treatment-experienced people

STANDARD DOSE

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

Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. Tablet should be swallowed whole; do not chew, crush, or split tablets.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

At the time of approval 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 antimycobacterial used for tuberculosis treatment, due to significantly reduced levels of fostemsavir. Cannot be taken with (contraindicated with) enzalutamide (an androgen receptor inhibitor), the anticonvulsants carbamazepine and phenytoin, the cancer drug mitotane, or the herb St. John's wort. Fostemsavir increases concentrations of statins (medications 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 (these abnormal heart rhythms can make the heart stop). Fostemsavir could affect oral contraceptive concentrations, especially those containing ethinyl estradiol. If a booster is not given in the regimen with fostemsavir, it may be co-administered with a combined oral contraceptive containing norethindrone and 30 mcg or less of ethinyl estradiol. It cannot be taken by trans women on estrogen hormone therapy due to the significantly increased risk for a blood clot. May increase levels of the hepatitis C virus (HCV) drugs grazoprevir and voxilaprevir; however, the magnitude of increase in exposure is currently unknown. Increased levels of grazoprevir may increase the risk of liver enzymes. Use an alternative HCV regimen if possible. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there may be other drug interactions which are not listed here.

MORE INFORMATION

Rukobia is a gp120 attachment inhibitor. A member of the drug class of HIV entry inhibitors, Rukobia works on the gp120 envelope protein that lies on the surface of the virus. It's a necessary part of getting the virus to enter the cell. Rukobia prevents attachment to the CD4 immune cell by blocking gp120 from binding to the CD4 receptor binding sites. This causes the virus to accumulate in extracellular space and is subsequently removed by the body's immune system. Very cool. Watch a video of its mechanism of action at youtu.be/WnreXE-TVi8. Rukobia is designed to be used in highly treatment-experienced people, who typically have fewer options for HIV treatment than those just beginning antiretroviral therapy. An option for treatment-experienced individuals is a good thing. "Even in the era of modern HAART [highly active antiretroviral therapy], antiretroviral [ARV] failure and resistance is still a problem worldwide," wrote HIV specialist Dr. Pedro Cahn and colleagues in *Current Opinion in HIV and AIDS* published July 2018. Dr. Cahn worked on fostemsavir research. Given that Rukobia does not appear to have cross-resistance to any currently approved antiretroviral, as well as its activity regardless of HIV tropism, it is a welcome new drug for people with very limited treatment options. Rukobia is active against CCR5, CXCR4, and dual-mixed virus (Selzentry is only active against CCR5). For individuals with HIV-2, commonly found in some other countries, Rukobia would not be recommended, as HIV-2 is inherently resistant to it. For more data, including medications added for optimized therapy, go to the FDA approval announcement at fda.gov/news-events/press-announcements/fda-approves-new-hiv-treatment-patients-limited-treatment-options. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

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 of note, including contraindications to administration with the androgen receptor inhibitor enzalutamide, some seizure 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 BRIGHTE 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.

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 multidrug-resistant virus in highly treatment-experienced people; but until those drugs are fully evaluated and approved, Rukobia remains an important tool in the HIV treatment toolbox.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$9,633.49/month

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Apretude

cabotegravir extended-release injectable suspension
CAB LA

PrEP **Long-acting PrEP (Pre-exposure Prophylaxis)** for the prevention of HIV

★ FDA approved 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 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 therapy has been missed, restart treatment with a 600 mg dose as soon as possible, followed a month later with another 600 mg dose, and then dose every two 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.)

- Oral cabotegravir is not available unless being prescribed cabotegravir LA.
- 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 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 approximately 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 result in lower protective levels of 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, herbals, 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 options 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, including viral suppression 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 STI testing, must be paid for by insurance carriers without co-pays or other cost sharing. GO TO bit.ly/dol-FAQ-ACA-part47. Insurers, however, may be more likely to insist that people on PrEP take the less costly generic version of Truvada. DHHS guidelines have a section on the use of cabotegravir for people with a history of injection drug use. Because cabotegravir has been detected in systemic circulation for up to 12 months or longer after the last injection, consideration should be given to potential for fetal exposure if prescribing cabotegravir to people of child-bearing potential who are not on birth control. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

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. Injection site 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 mind 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 immediately and fully scale-up 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 equity, the drug as well as 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.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com
(877) 844-8872

AVERAGE WHOLESALE PRICE

$4,440 per vial, based on WAC

Descovy for PrEP

emtricitabine/
tenofovir alafenamide
FTC/TAF

PrEP **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.

- SEE EMTRIVA, which is contained in Descovy. TAF is available separately as Vemlidy.
- SEE PACKAGE INSERT for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

The most common adverse event is diarrhea, observed in up to 5% of individuals given Descovy in the large DISCOVER study that led to FDA approval of Descovy for PrEP. There was also nausea (4%) and headache, fatigue, and abdominal pain (2% each). Check for hepatitis B virus (HBV) before taking Descovy and vaccinate against it if appropriate. If Descovy is discontinued abruptly in people with hepatitis B virus, flare-up of hepatitis may occur—talk to your provider before discontinuing. Drug resistance to HIV therapy may develop if people going on Descovy for PrEP unknowingly already have HIV, or if infection occurs after starting PrEP. However, drug resistance was rare in the extremely few individuals who acquired HIV during the DISCOVER trial (seven out of 2,670 persons on Descovy and 15 out of 2,665 on Truvada 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 and bones (such as decreases in estimated glomerular filtration rate, or eGFR, and bone mineral density, or BMD) when compared to TDF in Truvada. Kidney function (including creatinine clearance, or CrCl) should be monitored while taking Descovy for PrEP. Recommended monitoring also includes STI screening. When comparing TDF versus TAF, bone changes may be of greater concern for young people whose bone structure is still growing and for older individuals who may be becoming frail. Kidney changes may be of greater concern for individuals who have 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 Epclusa. Descovy should not be taken with certain anticonvulsants (including carbamazepine, oxcarbazepine, phenobarbital, and phenytoin), rifabutin, rifampin, rifapentine, or St. John's wort. Concentrations of tenofovir, FTC, and other substances that clear the body through the kidneys could be increased (along with risk of toxicity) by the aminoglycoside antibiotics and the antivirals acyclovir, cidofovir, ganciclovir, valacyclovir, and valganciclovir. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not.

MORE INFORMATION

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 preplocator.org and aidsvu.org—although any provider can prescribe PrEP. For more information, GO TO cdc.gov/hiv/basics/prep.html. Gilead Sciences helps people work with their insurance, including preauthorizations, 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: Rethinking HIV Prevention and 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 apregistry.com.

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 intensely controversial trial (full disclosure: I was an investigator) showed why robust community engagement in trial design and execution should not be bypassed by sponsors. The exclusion of cisgender women, transgender men, 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 STI screening) due to an "A" rating from the United States Preventative Services Task Force.

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.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

30-day blister pack: **$2,446.60**

Truvada for PrEP

emtricitabine/tenofovir DF
FTC/TDF

PrEP **Pre-exposure prophylaxis** (PrEP)

★ FDA approved for the prevention of HIV

■ GENERIC IS AVAILABLE

■ STANDARD DOSE

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

Take a missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. Truvada should not be used for prevention if CrCl or eGFR (measures of kidney function) is less than 60 mL/min.

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

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

■ POTENTIAL SIDE EFFECTS AND TOXICITY

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

■ POTENTIAL DRUG INTERACTIONS

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

■ MORE INFORMATION

Truvada for PrEP is 99% effective in preventing HIV when taken daily as recommended. Stigma and lack of access to health care continue to fuel HIV infections. Remember, risk depends on the situation—including where you live. Other problems include not knowing about PrEP and inability to perceive a need for it (not realizing one may have vulnerabilities at all). Although the drug label specifies prevention of sexually-acquired infection, U.S. HIV guidelines also recommend use for protecting against infection through injection drug use (reducing the risk of HIV by more than 70%, according to the CDC). The label notes that risk includes a number of behavioral, biological, or epidemiological factors, including condomless sex, current or past STIs, self-identified risk, having sexual partners of unknown HIV status or unknown HIV viremic status, or sexual activity in a high prevalence area or network. Screening and monitoring requirements include checking for STIs and 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-hiv-prevention. Two excellent websites for finding a PrEP provider are preplocator.org and aidsvu.org—although any provider can prescribe PrEP. Gilead Sciences helps people work with their insurance, including pre-authorizations, as well as provides free PrEP to uninsured people who are eligible, and co-pay assistance up to $7,200 a year; contact the patient assistance hotline 24/7 at (877) 505-6986, or go to gileadadvancingaccess.com. On-demand PrEP with Truvada, which uses four tablets around the time of sex, is supported by guidelines from the International AIDS Society-USA, the European AIDS Clinical Society (EACS), and the World Health Organization. Truvada generic became available in the U.S. in October 2020. See discussion online of the generic's pricing (positivelyaware.com/articles/briefly-novdec-2020 and positivelyaware.com/articles/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 allies. 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.

DR. MELANIE THOMPSON: Truvada was approved for PrEP in 2012 after being shown to be highly effective when taken with excellent adherence. The adherence challenges of taking a pill a day have always been its Achilles heel. Headache, abdominal pain, and decreased weight were the most common side effects attributable to Truvada in PrEP trials, and a few more people stopped drug for elevated creatinine or protein in the urine in the Truvada arm than the placebo arm. Bone density decreased more on Truvada than placebo, 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 screening) due to an "A" rating 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 cabotegravir (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 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 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.

■ 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

Egrifta SV tesamorelin for injection

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

STANDARD DOSE

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

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

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

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

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

Egrifta SV should not be administered to 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.

CAP & PAP INFORMATION

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

MANUFACTURER

Theratechnologies, Inc.
egriftasv.com

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

AVERAGE WHOLESALE PRICE

$7,789.20 for 30 2 mg vials

Mytesi crofemeler

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

STANDARD DOSE

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

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

Mytesi approval was based on a randomized, placebo-controlled study of 374 HIV-positive 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 decreased to 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 diarrhea for more than two years, have more than two watery bowel movements per day, and whose bowel movements tend to be "pourable" (not clumpy). Mytesi was less effective in African Americans in this clinical study.

An infectious cause should be ruled out prior to initiating Mytesi. In the placebo-controlled part of the study, side effects were comparable to placebo. The most commonly reported side effect was upper respiratory tract infection (Mytesi, 3.8% of 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.

CAP & PAP INFORMATION

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

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

Not available on formulary used

Serostim somatropin for injection

non-HIV | **Injectable human growth hormone** used for treating HIV-associated wasting in people on ART

STANDARD DOSE

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

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

CAP & PAP INFORMATION

There are several assistance programs, including the EMD Serono Secured Distribution Program, the AXIS Center, the Serostim Patient Assistance Program (PAP) or the Co-Pay Assistance Program (CAP). To find out more about these programs, call (877) 714-2947.

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

GO TO serostim.com, refreshed this year with more healthy living resources, injection tips, and advice for talking with your provider. See also hivwasting.com.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

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

HELP IS OUT THERE

HIV treatment can be costly, but there's help

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

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

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

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

Applying for PAPs

In 2012, the Department of Health and Human Services (DHHS), along with seven pharmaceutical companies, the National Alliance of State and Territorial AIDS Directors (NASTAD), and community stakeholders, developed a common patient assistance program application form that can be used by both providers and patients. This combines common information collected on

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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)

DRUGS COVERED	MANUFACTURER AND CONTACT INFORMATION	ASSISTANCE	RENEWAL
Kaletra and **Norvir**	**AbbVie** 800-441-4987, option 5; kaletra.com; norvir.com	**Kaletra:** Co-payment assistance covers up to the first $400 per prescription per month. **Norvir:** Covers up to $1,200 a year for co-payments.	
Atripla, **Biktarvy**, **Complera**, **Descovy**, **Emtriva**, **Genvoya**, **Odefsey**, **Stribild**, **Truvada**, **Tybost**, and **Viread**	**Gilead Sciences** 877-505-6986; gileadadvancingaccess.com	**Biktarvy, Descovy, Genvoya, and Truvada:** Covers the first $7,200 per year of co-payments. **Complera, 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.	Rolls over on January 1
Edurant, **Intelence**, **Prezcobix**, **Prezista**, and **Symtuza**	**Janssen Therapeutics** 866-836-0114; janssencarepath.com; edurant.com; intelence.com; prezista.com; prezcobix.com; symtuza.com	Covers the first $7,500 per year (for Symtuza, it's $12,500) of co-payments, deductibles, and co-insurance.	Automatic renewal
Delstrigo, **Isentress**, **Isentress HD**, and **Pifeltro**	**Merck and Co.** 800-444-2080; isentress.com	Covers the first $6,800 of co-payments, deductibles, and co-insurance for each of 12 eligible prescriptions.	Enrollment is valid until coupon expires, 12/31/2021
Trogarzo	**Theratechnologies** 833-238-4372; trogarzo.com; therapatientsupport.com	Contact program for details Worked out on a case-by-case basis	
Cabenuva, **Dovato**, **Juluca**, **Lexiva**, **Rescriptor**, **Retrovir**, **Rukobia**, **Selzentry**, **Tivicay**, **Tivicay PD**, **Triumeq**, **Trizivir**, **Viracept**, and **Ziagen**	**ViiV Healthcare** 844-588-3288; ViiVConnect.com	**Cabenuva**, $13,000; **Dovato** and **Juluca**, $6,250; **Tivicay**, $5,000; and **Triumeq** and **Rukobia**, $7,500 per year/per patient maximum. **Lexiva, Rescriptor, Retrovir, Selzentry, Trizivir, Viracept, and Ziagen:** $4,800 per year/per patient maximum.	Automatic renewal
Invirase and **Viread**	**Patient Access Network Foundation** 866-316-7263; panfoundation.org	Maximum benefit is $3,600 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.	Reapply each year

PATIENT ASSISTANCE PROGRAMS (PAP)

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

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

FOUNDATIONS

PROVIDING ACCESS TO CARE ASSISTANCE FOR PEOPLE LIVING WITH HIV

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

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

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

ADDITIONAL RESOURCES

THESE MAY BE OF INTEREST TO INDIVIDUALS LIVING WITH HIV

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

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

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

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

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

POZ ADVOCATE
SCOTT SCHOETTES
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The agony of defeat—and delayed drug development

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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