POSITIVELY AW

HIV DRUG GUIDE 2024

POSITIVELY AWARE

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LIVE LIFE POSITIVELY AWARE.
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TPAN was founded in 1987 in Chicago as Test Positive Aware Network, when 17 individuals 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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HIV DRUG GUIDE 2024

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EVERY ISSUE

THIS ISSUE

THE 28TH ANNUAL HIV DRUG GUIDE

‘Any excuse to celebrate is all you need’

Making living with HIV a celebration of life

New Orleans is rich in history and celebration. On the steps of the New Orleans Museum of Art, eleven HIV advocates came together for the cover photo shoot of this year’s annual HIV Drug Guide and shared their own experiences. Here are some of those personal stories, lightly edited and excerpted.

When I was diagnosed 15 years ago, I never dreamed that my life would be as magical as it is.

—Jimmy Gale

Jimmy Gale
(he, him), 39, public health professional and bartender

I’m a proud resident of the Upper Ninth Ward. This historic neighborhood has overcome a lot and survived its share of adversity. Around here, we take care of each other like family—after surviving hurricanes, tornadoes and floods together, *family* doesn’t even begin to describe it. Over here, we live on the porch and food is always meant to be shared. As a transplant to this amazing city, I’m so grateful to have landed where I did.

When I was diagnosed 15 years ago, I never dreamed that my life would be as magical as it is. I abruptly changed careers following my diagnosis to work in the field of HIV prevention and care. It led me to see the world through a different lens and eventually brought me to New Orleans. I immediately knew that this was where I was meant to be.

I am living with HIV due to sexual assault. I had to forgive myself long ago for something I had no control over. I always remind folks that we are much more than our diagnosis—you are still the same person and are worthy of every wonderful thing that comes your way.

Telling my mom was one of the hardest things I ever had to do. She raised three boys on her own and I was so afraid that she would be disappointed in me. Before I was diagnosed, I was heavily involved with HIV fundraising and education. So when I told Mom, her immediate response was, “Remember how passionate you were before all this... just think about what you can do now.”

My circle of friends was there for me as I navigated healthcare appointments and labs. They lifted me up as I learned how difficult disclosure and rejection can be. They reminded me who I was when I would fall into bouts of depression. Leaning on those that love you most can be scary, but I promise you that it’s worth it. Your hardest lessons eventually become a “how to” guide for others—so pay kindness forward and help newly diagnosed folks along their journey. For every moment you may have felt alone, you now have the power to help someone else feel loved.

This past October, I celebrated my fourth “NOLAversary” and am proud to call the Crescent City my home. Last year I was named Southern Decadence Grand Marshal, Gay Man of the Year

CAST PHOTOS: JOURDAN BARNES · ISTOCK

and was "sainted" by the Big Easy Sisters of Perpetual Indulgence. I represented my new home as Mr. Louisiana Leather at this year's International Mister Leather in Chicago. None of this would have happened if I hadn't been set on a different course. Living (and thriving) with HIV has reminded me to appreciate every wonderful thing that comes my way—and here in New Orleans, any excuse to celebrate is all you need.

Morris A. Singletary
(he, him), 47, community organizer and study recruitment coordinator

I found out on June 23, 2006 at 3:15 p.m. I had been super sick. I couldn't eat without throwing up. I was losing weight faster than I could eat. When I found out, I was afraid and felt disappointment in myself. I was shocked.

What's helped me live for more than 18 years have been God, my mom and the kids of my friends, who love and look up to me. The key is to let people love you, romantically and in friendship.

Cedric Sturdevant
(he, him) 58, executive director of Community Health PIER

I'm from a rural area in Mississippi called the Mississippi Delta. It's an area with a lot of richness, like farming, blues music, southern soulful cooking and Christian values. On the other hand, the Delta is also known for its lack of resources when it comes to HIV, including housing, transportation and adequate provider services.

Being a gay man and living with HIV, I never thought I would become an ordained minister, especially in the Mississippi Delta. I was ordained in June of 2022 by my pastor at Anointed Oasis of Love Ministry in Greenville, Mississippi. One goal I continue to pursue is educating and supporting Black boys and young men, whether or not they are part of the LGBTQ+ community. In my area, many Black boys and young men are growing up in unstable housing, without a father in their lives. I try to be a mentor figure.

Jen Laws
(he, him), 38, trans man, president and CEO of Community Access National Network, public policy analyst

I was diagnosed in 2004 on my first test. It was a routine part of my medical care as a young queer adult looking for my first "grown up" doctor on my own.

Despite a decent amount of education on HIV at the time, the very first moments felt like a movie happening outside of myself. I'm not sure I even heard what my provider was telling me after sharing the diagnosis with me. I don't remember much of the day after the appointment. It took me years to rid myself of some unreasonable fears about my own health and for the health of my partner, but I overcame them eventually.

> My motto is, ***Try something new every week***— and I do just that! I appreciate life and do not take it for granted.

I think anyone facing a life-changing diagnosis needs time, regardless of how manageable that diagnosis might be. Distance from that traumatic moment helps. And in that distance, I found a lot of love and support and a whole lot of folks who didn't make a big deal about my status. Not that they didn't care, but that it did not affect their affection for me or their desire to be friends.

It's gonna feel lonely from time to time. And that's OK. Our purpose in this life is to help each other feel a little less alone and to seek out the people who help us feel less alone. Give it time, shift your effort some maybe, and you'll find more of your people around you.

I want to end on the thing I struggled with the most: God loves you, in all your glory. You were made in the image of the Divine, which makes you Divine. This virus cannot change that fact. Anyone who struggles to love you is merely working out their struggle in their connection to God and that's not yours to carry. You just love them through it, even if that means from a distance. Because the closer you get to settling yourself in that Divinity, the more connected to It and yourself you'll be. You got this. And I love you.

W. Miller
(he, him) 69, retired surgical technologist

The neighborhood I call home is Gentilly Terrace, located in the 8th ward. It was the first residential area built on hills and contains a series of Craftsman homes, each uniquely designed.

When I was diagnosed January 2, 2000, my response was one of shock. I was numb. I did nothing for almost a year. After talking with a close friend, I decided to get onto antiretroviral treatment. I made an appointment with the HIV clinic at the University of California-San Francisco (UCSF) medical center. A new young doctor at the time, Malcolm John, prescribed my medication and enrolled me in a program he was starting, The Men of Color. I listened to Dr. John and I'm still here! My support systems have been a series of wonderful health care providers starting with the UCSF HIV clinic and now here in New Orleans with the caregivers and medical team at Crescent Care.

I've enjoyed 17 years with a wonderful man who is now in heaven but forever with me in my soul. He saw something in me and gave me the pleasure of sharing his life with me knowing I was living with HIV.

HIV does not feel like a barrier to life, thanks to the medication that keeps me undetectable—and untransmittable. Life has given me a chance to explore new experiences. My motto is, *Try something new every week*—and I do just that! I appreciate life and do not take it for granted. At 69 I expect to live and make every effort to live another 31 years—after that, I'll renegotiate.

—COMPILED BY **RICK GUASCO**

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Picture yourself

When you are in an agency working and you randomly see your favorite magazine, POSITIVELY AWARE, and then you flip through and see your photo from A Day with HIV.

—CHAD HENDRY
VIA FACEBOOK

'Webale nnyo'

In our country, Uganda, a lot of Ugandans have been attacked since the [anti-homosexuality] law was passed. People from outside countries who are allowed to be themselves, you give us courage to fight for our rights. In my local language we say, *Webale nnyo*—thanks so much.

—NAME WITHHELD

Laughing matters

A much-needed new direction... Yayyy!

—DORIAN-GRAY ALEXANDER

I wish to inform you that I was granted parole after 37 years of confinement at Sullivan Correctional Facility, and shall be returning to western Africa before the end of this month. My sincere gratitude to all the staff at POSITIVELY AWARE, who have been keeping us informed. I intend to continue my work in viral epidemic education, prevention and counseling.

—MAURICE POBLAH
NEW YORK

EDITOR'S NOTE

Rick Guasco
@rickguasco

'Book of hope'

In difficult times, I look for hope. And when there's hope, there is reason for celebration. I find hope in how far we've come in HIV prevention and treatment. But I'm also pragmatic.

Information is the key to hope. I like to think that the annual POSITIVELY AWARE HIV Drug Guide is a "book of hope." In addition to the HIV drug pages (21–61) that provide details on dosing, side effects and drug interactions, what makes these pages unique are the insightful, candid comments about each drug from an HIV specialist, Dr. Melanie Thompson, and a patient advocate, Joey Wynn. Special appreciation to Eric K. Farmer, PharmD, for updating the drug pages and to my colleague, associate editor Enid Vázquez, for her work on them. And a shout out to art director Greg Mytych for making the HIV drug guide user friendly and appealing.

Also inside, contributing writer Larry Buhl's *Guide to long-acting injectables for HIV* (page 16) looks at the different LAIs, outlining who the drug has been approved for—and who it's not for. "Help is out there" (page 62) lists all the nonprofit organizations and pharma assistance programs that help people pay for their HIV meds. When it comes to the power dynamics of the doctor-patient relationship, Bridgette Picou asks, "Are clinicians listening?" (page 65). Bridgette follows up in her column (page 68), suggesting that care providers must build trust if patients are to have faith (or hope) in their treatment.

What better city to photograph the HIV drug guide's cover than in New Orleans, a city that knows how to celebrate?

Let the good times roll, as New Orleans' motto says, roughly translated from its original Cajun-French, *Laissez les bons temps rouler.* The city is rich in history, diverse cultures and close-knit communities that have overcome so much.

"I'm a proud resident of the Upper Ninth Ward," says Jimmy Gale, one of the people living with HIV featured in the Behind the Cover feature (page 4). "This historic neighborhood has overcome a lot and survived its share of adversity. Around here, we take care of each other like family—after surviving hurricanes, tornadoes and floods together, *family* doesn't even begin to do it justice."

But it's not all good times.

According to the quarterly report of the Louisiana Department of Health's Office of Public Health STD, HIV and Hepatitis Program, as of this past March 31, there were 23,126 people were living with HIV in the state—10,969 (47%) of them were diagnosed with late-stage HIV, sometimes referred to as AIDS.

Of the 875 Louisianans who were newly diagnosed in 2023, Black people accounted for 68% of the HIV diagnoses and 69% of the late-stage (or AIDS) diagnoses. Louisiana's overall population is 32% Black. Among the most vulnerable groups, 60% of new HIV diagnoses last year were Black men who have sex with men. People ages 25–34 comprised 34% of new diagnoses; 24% were ages 13–24.

This, in a state that still has a 1987 law criminalizing HIV. If convicted under the law, a person can face up to 10 years in prison and registration as a sex offender for up to 15 years.

It's a long, slow process, but efforts are underway to modernize the law. In late 2023, the Louisiana Coalition on Criminalization and Health conducted a study that in part measured public attitudes today about HIV. The opinion survey found that 93.5% of respondents believed the law needs updating; 87% agreed that the law does not make sense, based on the medical principle of undetectable equals untransmittable (U=U)—a person who is on HIV treatment and whose viral load is undetectable by most tests, is *incapable* of passing on the virus to their sex partner.

There's reason for hope.

You are not alone.

Rick

P.S. As I write this, the National AIDS Manual and its website, aidsmap.org, **announced they will cease operations this summer after 37 years**. Based in London, they have been one of the world's leading independent community-based sources of accurate and trusted HIV information. With heartfelt loss, PA's staff salutes our colleagues at aidsmap.

A friend asked if this meant that HIV was no longer a serious thing. *No*, I said. It means that funding sources for HIV information are drying up. HIV is still here. We were starting to think that HIV was little more than a "chronic condition" that could simply be managed by taking one pill a day or a shot or two every couple of months or so, and that that was all we needed to know. But we keep discovering there are long-term effects of HIV, inflammation related to HIV and that co-existing conditions and aging are exacerbated. *No*, I said. We need our sources of HIV information as much as ever.

JOHN GRESS · ILLUSTRATION: ISTOCK

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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. 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 living with HIV in Atlanta since that time.

She currently co-chairs the HIV Medicine Association (HIVMA) HIV Primary Care Guidance Panel that 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

Joey Wynn is a 58-year-old gay man, deeply entrenched in Florida's state-level HIV advocacy and HIV care since 1991. Chairman of the South Florida AIDS Network (SFAN) for almost 20 years, he advocates to local, state and national leaders on policy recommendations and priorities from the local HIV community. Joey believes that difficult decisions are made balancing the needs of people living with HIV with the financial impact to the service delivery system in a limited, financially constrained environment. With an ultimate passion to maintain state AIDS Drug Assistance Programs (ADAPs) at their highest functional abilities that must work for all sectors of the community, he has firsthand experience with several of the drugs described in this guide, reaching out throughout the year, listening and learning from hundreds of others about their medical journeys and personal experiences with HIV-related medications.

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 worker and transgender communities.

THE EDUCATOR

Carla Blieden, PharmD, MPH, AAHIVP, reviewed the Department of Health and Human Services (HHS) guidelines for this drug guide. Dr. Blieden 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.

FARMER AND VÁZQUEZ: JOHN GRESS • BLIEDEN: ISAAC MORA

More than HIV

During a doctor's appointment, there's not always the opportunity to tell your care provider everything. So, POSITIVELY AWARE asked our social media followers:

What's the one thing you wish your doctor or care provider knew about you and about treating your HIV?

COMPILED BY **RICK GUASCO**

"As long-term survivors we are dealing with multiple comorbidities and providers need to be able to treat your HIV while understanding your other health issues to avoid medication conflicts or side effects that may exacerbate your other health issues."

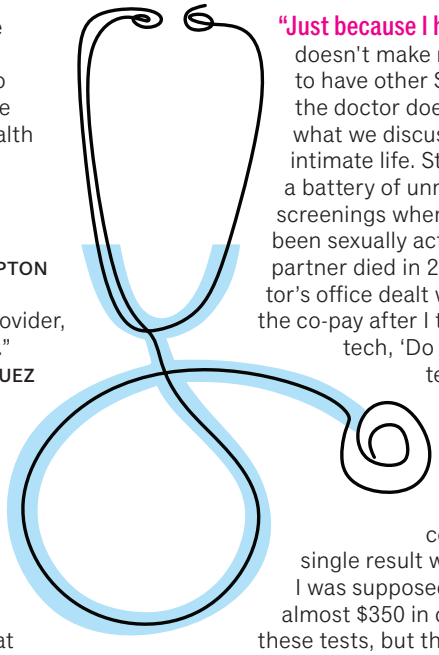
—LARRY FRAMPTON

"I share everything with my provider, past and present. Everything."

—MARIO MARQUEZ

"I was told one time by a physician assistant that I had 15 minutes to talk. I told her that if she would be quiet then I could tell her my issues that I was experiencing. Bedside manner and cultural competence are necessary to treat me now that I'm in my 50s."

—JACK R. MILLER



"Just because I have HIV doesn't make me more likely to have other STIs. It implies the doctor doesn't believe what we discuss as to my intimate life. Stop ordering a battery of unnecessary STI screenings when I have not been sexually active since my partner died in 2016! The doctor's office dealt with paying the co-pay after I told the lab tech, 'Do not run these tests—they are unnecessary and inappropriate.' And she did anyway. (Of course, every single result was negative.) I was supposed to pay almost $350 in copays for these tests, but they are dealing with it now."

—XIO MORA-LOPEZ

"Doc, I've lived a long time with this... what do we need to do to keep it up?

—GREG KNEPPER

"Many people experience diarrhea, which can be caused by medication or by HIV itself. I discovered something by accident. I never thought about being lactose intolerant. I switched from regular milk to lactose-free milk. Ten days later, my diarrhea almost stopped. Such a simple thing, doctors should ask about this simple change."

—JIMMY ONTIVEROS

"I wish my MDs would treat me like an 80-year-old man in a 65-year-old's body. That reality doesn't make sense to them because I don't look 15 years older. [But] I wake up every day feeling like I have an 80-pound sack of potatoes on my shoulders. That's what premature aging does to you."

—JAMES CHANDLER HOVEY

"@Xio Mora-Lopez: "Unfortunately, if any of your care is paid for by Ryan White funds (including 'just' case management), annual screening at least for syphilis is a required/reported quality measure, and there is no opt-out/exclusion in the tabulation for those who report not being sexually active. That being said, you absolutely have the right to manage co-pay issues, and they do have to have your consent to run any labs. I know from monitoring lab results in our clinic that a surprising number of positives come back on those who report having 'no sexual activity,' which is the justification many offices use, but it is never acceptable to go against a patient's expressed instructions."

—MICHAEL LUCIANO

"Sometimes I just need to go over my medical history and us both just laugh. I know I've beat the odds and I'm still here fighting. Makes for one hell of a story."

—DEREK CANAS

"The fact that I stand before you today because of HIV does not mean that HIV is the only thing that determines my life. I am a human being with preferences, thoughts, political views, relatives and beliefs, and HIV is not something that defines me. I'll just take the treatment I need and get on with my life the way I started it. So, whatever you think about HIV, any feedback you give me should be unbiased and purely scientific. (This is a common opinion based on the feedback we have received from all our counselees for about 10 years.)"

—@REDRIBBON

"I am a WHOLE person, not separate parts, parceled off to different doctors. Everything in and on me is connected to everything else. Know about, care about, and treat the entire person."

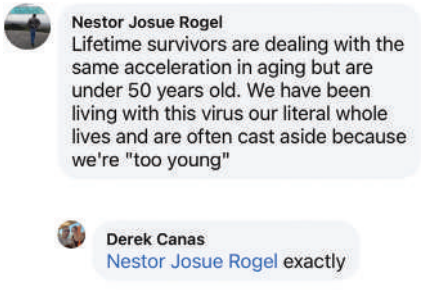
—BRIAN OLSEN

"I can't think of anything my current primary/ID fellow and her preceptor (supervisor) don't know about my HIV treatment history, thanks to the extensive meds chronicles I brought to my first appointment. They appreciate my pharmacology knowledge and had no problem allowing me to drive a meds change when my viral load got blippy last fall due to the lactose-based binder in Odefsey."

—DAVIDMICHAEL PHILLIPS

"Sometimes the provider needs to listen to the concerns of the person living with HIV without interruption."

—TIMOTHY S. JACKSON



"I worry that what happens (hearing loss, arthritis, etc.) is 'normal' aging for someone in his mid-50s or is it accelerated aging brought on by nearly 30 years of constant inflammation brought on by HIV."

—ERIC MOORE

ILLUSTRATION: ISTOCK · @NGUPAKARTI

Briefly

ENID VÁZQUEZ @enidvazquezpa

Biktarvy now recommended for pregnancy

For years the POSITIVELY AWARE HIV Drug Guide has reported that, "There aren't sufficient data to support the initiation of Biktarvy during pregnancy." We went on quickly to explain that, "People who become pregnant while on Biktarvy do not necessarily have to switch to another regimen, but may undergo closer monitoring of viral load."

Now it's official: Biktarvy can be used in pregnancy. This is important because Biktarvy is a recommended regimen for most people living with HIV and one of the most commonly prescribed HIV medications in the U.S. It is a single-tablet regimen, taken as one daily pill for complete HIV treatment.

In January, the Department of Health of Human Services (HHS) perinatal HIV treatment guidelines upgraded its Biktarvy recommendation from "insufficient data to recommend" to an "alternative drug" for use in pregnancy or around the time of conception.

Then in April, the U.S. Food and Drug Administration (FDA) approved a change to the Biktarvy package insert (PI, also known as the drug label), adding new pregnancy data.

Still, **pregnancy does have the effect of lowering blood levels of Biktarvy—something that's already known—and closer monitoring of viral load is recommended.**

HHS

"Based on new data about pharmacokinetics [basically, how drugs are processed in the body] in pregnancy and updated information in the Antiretroviral Pregnancy Registry, bictegravir (BIC) is now recommended as an *Alternative* ARV [antiretroviral] for use in pregnancy and for people who are trying to conceive; it was previously categorized as *Insufficient Data to Recommend* use in pregnancy. Data are still limited, but no safety concerns have been observed," the HHS perinatal guidelines panel of experts reported in January.

Lower blood levels of Biktarvy in pregnancy were "not considered clinically significant in virologically suppressed pregnant individuals," HHS guidelines said. The upgraded recommendation thus applies to people with undetectable viral loads—less than 50 copies per mL. That's the number one goal of HIV treatment—getting to undetectable.

Having an undetectable viral load, however, nearly always requires HIV medication. Therefore, the upgraded rating for Biktarvy implies that anyone with HIV who hopes to become pregnant should consider being on HIV treatment first, whether on Biktarvy or on another medication. HHS perinatal guidelines strongly recommend HIV therapy for positive pregnant individuals.

At any rate, the upgrade is a reassuring advance in evidence-based HIV treatment.

Gilead Sciences

The maker of Biktarvy presented the FDA with data from Study 5310, which reviewed the safety, efficacy and pharmacokinetics of Biktarvy in pregnancy.

"This label update marks an important milestone for Biktarvy, reinforcing its efficacy profile for pregnant PWH [people with HIV], an often understudied and most vulnerable community in clinical research," said Jared Baeten, MD, PhD, vice president of HIV Clinical Development at Gilead Sciences, in a press release. "Not only is Biktarvy an alternative regimen for use in pregnancy, but people of childbearing potential can also remain on Biktarvy if they become pregnant."

The Biktarvy label was also updated in February to include the breastfeeding/chestfeeding guidance from the U.S. Centers for Disease Control and Prevention, which urges doctors to work with positive pregnant people in deciding whether they want to breastfeed or chestfeed.

In Study 5310, the 32 participants who completed the study remained undetectable throughout pregnancy and through 18 weeks after giving birth. The 29 infants born during the study remained HIV-negative out to eight weeks following birth.

"This update makes Biktarvy the only second-generation integrase strand transfer inhibitor (INSTI)-based single-tablet regimen (STR) with in-label clinical trial data and FDA approval in virologically suppressed adults who are pregnant," Gilead reported.

As stated by HHS guidelines, the label says that pregnant individuals must have undetectable viral load before going on Biktarvy, on a stable HIV regimen, and have no drug resistance to any of the three medications found in Biktarvy.

GO TO clinicalinfo.hiv.gov.

ISTOCK

TOP OF THE NEWS

➤ Biktarvy now recommended for pregnancy ➤ Preferred HIV medications for pregnancy ➤ Center for Black Equity names interim CEO ➤ CDC issues guidelines for using doxy-PEP against STIs ➤ From the *NIAID HIV Language Guide* ➤ NIAID updates HIV language guide ➤ Sluts: new book takes on PrEP shaming ➤ CDC reports new HIV statistics ➤ FDA approves HPV self-collection kit

Preferred HIV medications for pregnancy

"All pregnant people with HIV should initiate antiretroviral therapy (ART) as early in pregnancy as possible, regardless of their HIV RNA [viral load] level or CD4 T lymphocyte cell count, to maximize their health and prevent perinatal HIV transmission and sexual transmission," according to the perinatal HIV treatment guidelines from the U.S. Department of Health and Human Services (HHS).

The HIV medications listed here are recommended by the expert panel behind the perinatal guidelines for use during pregnancy or conception by people taking HIV treatment for the first time (called *treatment-naïve*). SEE Table 6 of the guidelines. Table 6 also includes a list of what not to take. SEE Table 7 of the guidelines for recommendations for people who are already taking HIV therapy. Both tables list advantages and disadvantages of the medications, as well as special considerations. See other sections of this POSITIVELY AWARE HIV drug guide issue for information on these medications and their drug classes.

Note that according to the guidelines, "In general, the Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission (the Panel) recommends that people who are already on fully suppressive [undetectable viral load] ARV regimens when pregnancy occurs should continue with those regimens, unless they are receiving an ARV drug or ARV regimen that is not recommended for use in nonpregnant adults or concerns exist about safety and inferior efficacy during pregnancy (SEE Table 7.)."

To see the *Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States*, GO TO clinicalinfo.hiv.gov.

Preferred drugs

Preferred INSTI regimens
Triumeq *or* Tivicay plus a preferred dual-NRTI backbone

Preferred PI regimens
If pregnant person has used Apretude, Prezista boosted by ritonavir plus a preferred dual-NRTI backbone

Preferred dual-NRTI backbone medications
Epzicom
Descovy *or* Vemlidy plus Epivir
Truvada *or* Viread plus Epivir

Alternative drugs

Alternative INSTI regimens
Biktarvy
raltegravir 400 mg twice daily (SEE Isentress on page 41) plus a preferred dual-NRTI backbone

Alternative PI regimens
Prezista twice daily boosted by Norvir plus a preferred dual-NRTI backbone
Reyataz boosted by Norvir plus a preferred dual-NRTI backbone

Alternative NNRTI regimens
Atripla or Symfi or Sustiva plus a preferred dual-NRTI backbone
Complera or Odefsey or Edurant plus a preferred dual-NRTI backbone

Alternative dual-NRTI backbone medications
Combivir (considered a legacy drug in this drug guide issue and no longer appears in the drug pages; an FDC - fixed-dose combination of AZT and Epivir)

NOTE: Two-drug regimens are not recommended for initiation of ART in pregnancy due to a lack of data.

FDA approves HPV self-collection kit

Roche Pharmaceuticals announced the approval of its new self-collection kit for human papilloma virus (HPV) by the U.S. Food and Drug Administration (FDA). It is one of the first approved by the FDA.

"Screening for HPV can help identify women who are at risk of developing cervical cancer so that the disease can be found and treated early before cervical cancer has a chance to develop," Roche announced in a May 15 press release.

A positive result for HPV requires follow up with a provider.

Cervical cancer occurs more often in women living with HIV than among other women. It is an AIDS-defining condition. Most people in the U.S. who have had sex will acquire HPV, of which there are more than 100 strains.

"More than half the patients diagnosed with cervical cancer in the U.S. have never been screened or have only been screened infrequently, and they do not participate in routine screening," Roche reported. "Many factors can contribute to individuals not participating in cervical cancer screening programs, such as access to healthcare, social and economic barriers, history of traumatic experience, cultural concerns and embarrassment. Roche's self-collection solution can help reduce these barriers by offering an alternative to clinician collection procedures, while also providing accurate and

reliable results enabling clinicians to make patient care decisions."

Roche is working with the Cervical Cancer 'Last Mile' Initiative of the U.S. National Cancer Institute.

GO TO prevention.cancer.gov/major-programs/nci-cervical-cancer-last-mile-initiative.

"With vaccinations, innovative diagnostic tools and screening programs, achieving the [World Health Organization's] goal of eliminating cervical cancer by 2030 is within reach," said Matt Sause, CEO of Roche Diagnostics. "Our HPV self-collection solution helps support this goal by reducing barriers and providing access to HPV screening by allowing people to privately collect their own sample for HPV testing."

Center for Black Equity names interim CEO

The DC Center for AIDS Research (DFAR) announced that Kenya Hutton, a member of its Community Partnership Council, has been named interim CEO and president of the Center for Black Equity. The mission of CBE is to "promote a multinational LGBTQ+ network dedicated to improving health and wellness opportunities, economic empowerment and equal rights while promoting individual and collective work, responsibility and self-determination." CBE focuses on three areas: economic equity, social equity and health equity. Within the health arena, CBE focuses on "allowing Black LGBT people to thrive physically, behaviorally, environmentally and spiritually."

Hutton has served as CBE's deputy director for four years, and in other capacities for a decade before that. He succeeds founding CEO and president Earl Fowlkes, Jr. Although retiring after 25 years, Fowlkes will continue to serve the global organization in an advisory capacity as CEO/president emeritus.

In a separate announcement, CBE described Hutton as "a seasoned leader with a proven track record in advancing racial justice initiatives." GO TO centerforblackequity.org.

New HHS recommendations on anal cancer screening in HIV

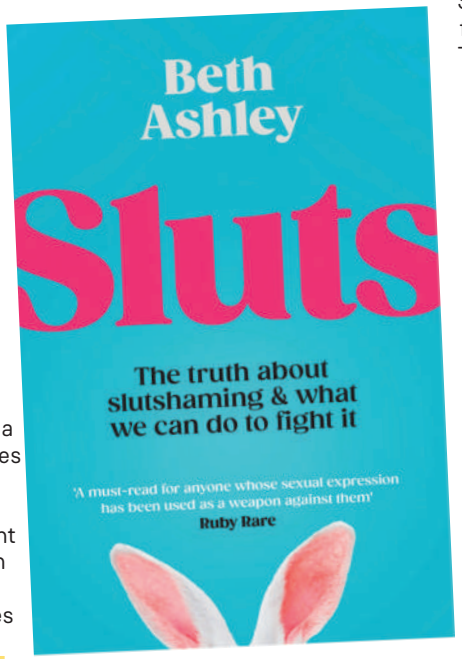
U.S. HIV treatment guidelines added new recommendations for anal cancer screening and prevention thanks to the ANCHOR study. "These recommendations include a screening program that uses high resolution anoscopy (HRA) to help detect and treat precancer and prevent anal cancer for people with HIV," the Department of Health and Human Services reported. "The guidelines recommend that **all adults with HIV be assessed at least once per year for anal abnormalities** (such as pain, burning or masses) and undergo digital anorectal examination (DARE).

"People under the age of 35 who are symptomatic or show signs of anal cancer (visual or palpable abnormalities) during DARE should undergo standard anoscopy.

"Older people should undergo additional lab-based screening with subsequent HRA, rather than standard anoscopy, if they are among the following populations:

- Men who have sex with men and transgender women ages 35 and older
- All other people with HIV ages 45 and older

"This lab-based screening should include collection of anorectal specimens for diagnosis," wrote HHS in July. "If there are any abnormalities on those specimens, or symptoms or signs of anal cancer in the initial assessment and DARE, clinicians should make a referral for HRA." GO TO clinicalinfo.hiv.gov.



Sluts: new book takes on PrEP shaming

London-based writer Beth Ashley, editor-in-chief of *Paperfox* literary magazine, has written *Sluts: The Truth about Slutshaming and What We Can Do to Fight It*. In an excerpt at *Gay Times*, a global online news and lifestyle magazine based in Great Britain, she writes, "**The slutshaming around PrEP has the potential to overshadow its scientific accomplishment** and even 'cloud the judgement of medical providers, policymakers, insurers and potential PrEP users,' according to the 'PrEP Whores' research. Essentially, the availability of PrEP could be affected by the slutshaming that surrounds it, as lawmakers and governing bodies could deem it a 'dirty' device for promiscuity and see it as less of a priority."

Or, as the *Gay Times* subhead says, *PrEP slutshaming is still alive and well—and it's harming us all.*

Ashley goes on to quote people on PrEP and HIV prevention and treatment advocates, including individuals working on behalf of the LGBTQ+ community. She also covers research findings around HIV PrEP. The book launch was held in May.

To read the excerpt, GO TO gaytimes.com/life/prep-slutshaming.

CDC reports new HIV statistics

In May, the U.S. Centers for Disease Control and Prevention (CDC) issued its latest statistics on HIV incidence and prevalence.

According to the HIV + Hepatitis Policy Institute, "CDC data released today [May 20] show that the number of **new HIV diagnoses in the United States remained stubbornly stable at 31,800 in 2022**. While new HIV diagnoses have fallen by 12 percent over the past five years, driven by a 30 percent decrease in new cases among young people, the number remains high and is not decreasing at the rate needed to end HIV by 2030."

For transgender women, diagnoses increased by 25 percent. Latino gay men now account for 39 percent of all HIV diagnoses among men who have sex with men. GO TO hivhep.org.

Estimated HIV Incidence and Prevalence in the United States, 2018–2022 is a supplemental report of the CDC's HIV Surveillance Report. CDC explained that incidence refers to "the number of infections during a specified time" and prevalence refers to the number of people living with HIV at a given time, regardless of when they acquired the virus or were diagnosed.

GO TO cdc.gov. DOWNLOAD the supplemental report at stacks.cdc.gov/view/cdc/156513/cdc_156513_DS1.pdf.

Updated OI guidelines

The Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV were **updated in May regarding the treatment of mycobacterium tuberculosis**.

According to the update, the guidelines:

- Recommended a 4-month regimen of daily rifapentine, isoniazid, pyrazinamide and moxifloxacin as an alternative treatment for active pulmonary tuberculosis (TB) in people receiving efavirenz-based antiretroviral therapy.
- Recommended a regimen consisting of bedaquiline, pretomanid, linezolid, and moxifloxacin (BPaLM) as the preferred treatment for rifampin-resistant TB.

As with the adult and adolescent treatment guidelines and the perinatal guidelines, the OI guidelines are produced by the Department of Health and Human Services. Note: efavirenz-based treatments are rarely prescribed in the U.S. today.

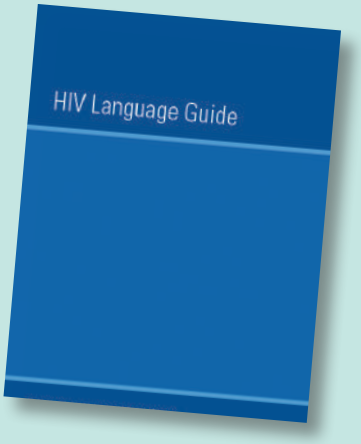
GO TO bit.ly/3KDRq6L.

CDC issues guidelines for using doxy-PEP against STIs

It's official. The U.S. Centers for Disease Control and Prevention (CDC) has issued guidelines for preventing STIs through the use of doxy-PEP. "In three large randomized controlled trials, 200 mg of doxycycline taken within 72 hours after sex has been shown to reduce syphilis and chlamydia infections by greater than 70% and gonococcal infections by approximately 50%," the CDC reported. The recommendation is to take 200 mg doxy within 72 hours after a sexual exposure, real or potential, and no more than 200 mg every 24 hours. **Specifically, providers should offer the option of a doxy prescription to men who have sex with men and transgender women** who have had a bacterial STI (specifically syphilis, chlamydia or gonorrhea) diagnosis within the previous 12 months, because they are the groups most affected by the growing rate of STI cases. A doxy prescription should be enough to cover the number of anticipated sexual encounters before the next clinic visit. The need for doxy-PEP (post-exposure prophylaxis) should then be assessed every 3 to 6 months, along with STI testing. "We will continue to adjust our recommendations as additional data are available," the CDC stated.

GO TO bit.ly/3VWEYFC.

NIAID updates HIV language guide



The National Institute of Allergy and Infectious Diseases in April updated its HIV language guide. NIAID said it **strove to eliminate language and terminology considered "offensive and stigmatizing."** NIAID also announced a campaign to "educate and strongly advocate for person-first, non-stigmatizing language in all of our communications, including but not limited to grant applications, contracts, publications, presentations, abstracts and press materials." SEE "A call to end stigmatizing language in HIV research" in the FEB+MAR issue; GO TO bit.ly/4eA7K6z. See sidebar.

From the *NIAID HIV Language Guide*

Emphasizing use of Non-stigmatizing, Person-First Language

Do not describe people by their disease, infection or condition; use instead:

- People with HIV rather than HIV-infected people
- People who inject drugs rather than injection drug users

Do not use *subjects* or *patients* to describe people enrolled in research studies or clinical trials; use instead:

- Participant
- Volunteer

Do not use 'sex' and 'gender' interchangeably:

- Sex (refers to sex assigned at birth)
- Gender (refers to psychosocial or cultural identity)
- Use *cisgender* for people whose gender matches their sex assigned at birth and *transgender* for people whose gender does not match their sex assigned at birth

Do not use *at risk* or *high-risk* to characterize a person, use instead:

- Person/population with greater likelihood of HIV exposure
- Population experiencing a disproportionate impact of HIV
- High-incidence population
- Affected community

Do not use *sterilizing* when referring to HIV cure; use instead:

- Elimination
- Eradication
- Clearance

GO TO niaid.nih.gov/research/hiv-language-guide

GUIDE TO LONG-ACTING INJECTABLES FOR HIV

BY **LARRY BUHL**

Long-acting injectable (LAI) medications for HIV treatment have much longer half-lives than oral medication, meaning the drug stays at a high enough level in the blood to suppress HIV. Right now, there are three injectable medications approved for treatment of HIV, however, each is used differently:

- cabotegravir and rilpivirine
- lenacapavir
- ibalizumab

Each injectable regimen has its own indications and benefits (and restrictions). People with HIV should consult with their doctors to see whether switching from daily oral meds to any of these injectables would be beneficial.

Cabotegravir + rilpivirine (Cabenuva)

Cabotegravir is an integrase strand transfer inhibitor (INSTI) and is used in combination with rilpivirine, which is an NNRTI (a non-nucleoside reverse transcriptase inhibitor).

In North America and Australia, the injectable combination of these drugs is packaged under the brand name Cabenuva. In Europe, the brand name is Vocabria. Cabotegravir and rilpivirine are administered as two separate injections into the buttock muscles a few minutes apart by a clinician (usually a nurse or doctor). Cabotegravir and rilpivirine (CAB/RPV) can be taken either once a month or every two months. Taking the pill form of these meds for the first month to see if there's any negative reaction before starting injections is called a "lead in." It is optional, although most people opt to begin receiving injectable treatment right from the start.

Who can take CAB/RPV?

Injectable cabotegravir and rilpivirine are approved for adults and youth:

- with a viral load under 50 who are already on a stable oral antiretroviral regimen
- without resistance to integrase inhibitors or NNRTIs

CAB/RPV is *not*, at this time, for:

- people with a detectable viral load
- people who are starting HIV treatment; a person needs to first take an oral antiviral for a few months to achieve an undetectable viral load before switching to an injectable treatment
- children under age 12 (although trials of children under 12 are ongoing)
- people during pregnancy or who are breastfeeding/chestfeeding (though trials for these groups are ongoing)
- people with a strain of HIV called A6
- people with a body mass index over 30 or with buttock implants, which may decrease the ability of the drugs to get into the bloodstream

Injectable cabotegravir and rilpivirine may also have negative reactions for people taking:

- anticonvulsants, including carbamazepine, oxcarbazepine, phenobarbital and phenytoin
- antimycobacterials rifabutin, rifampicin and rifapentine
- the glucocorticoid dexamethasone
- the herbal supplement St. John's wort

Cabenuva injections are safe for people using gender-affirming hormones, and for people using contraception meds.

Lenacapavir (Sunlenca)

Approved by the FDA in 2022, lenacapavir (LEN) is the longest-acting injectable treatment for HIV, and it's approved in the U.S., U.K., Canada and the EU under the brand name Sunlenca. Lenacapavir is an HIV capsid inhibitor, which interferes with the HIV capsid, a protein shell that protects HIV's genetic material, and can be very effective against HIV that has developed resistance to other drug classes. Because lenacapavir stays in the body for a very long time, injections are only done twice a year.

However, LEN must be used in combination with other HIV meds, usually daily pills. This is a difference from cabotegravir+rilpivirine, which is effective as (monthly or bi-monthly) injections alone.

Lenacapavir treatment starts with oral dosing to establish stable blood levels. The recommended oral dose is 600 mg on day 1 and 2, then one 300 mg tablet on day 8. Assuming all goes well, 927 mg may be given via injection on day 15.

Lenacapavir is approved for:

- people who have taken many other HIV meds and have multi-drug resistant HIV and have limited treatment options
- people who are unable to achieve viral suppression on their current regimen

Lenacapavir is *not* for:

- treatment-naïve people with HIV (people who have never been on HIV meds before)
- pregnant people and children under 18 years (because it hasn't been studied in these groups)

Lenacapavir is also being evaluated as a first-line treatment and as pre-exposure prophylaxis (PrEP).

Ibalizumab (Trogarzo)

Approved by the FDA in 2018, ibalizumab is a monoclonal antibody given as an injection every other week. Like lenacapavir, it must be taken in combination with other meds. It is for heavily treatment-experienced people whose HIV cannot be treated successfully with other currently available meds.

Who can take Trogarzo?

Trogarzo is for adults with HIV who:

- have taken HIV medications in the past
- have HIV that is resistant to other antiretrovirals

ISTOCK

- are failing their current regimens

Trogarzo is *not* for:

- people with hypersensitivity reactions including infusion-related reactions and anaphylactic reactions
- people who have never been on any HIV treatment.
- children; there aren't enough data to determine if Trogarzo is safe and effective for kids

Although there aren't adequate data to determine whether Trogarzo may have risks during pregnancy, other monoclonal antibodies could be transmitted from the pregnant parent to the developing fetus. Based on animal data, infants born to mothers taking Trogarzo during pregnancy could have reversible immunosuppression.

Benefits of long-acting injectables

Based on randomized controlled trials, LAIs for HIV treatment are just as effective as daily pill regimens in bringing the viral load to an undetectable level. A main benefit, in theory, is the ease of adherence, although there are not enough data to conclude this. And it should be noted that in clinical trials, cabotegravir and rilpivirine were given to participants who already had good adherence to daily meds.

People who don't want a daily reminder of their HIV status, or who want to keep their HIV status private, might benefit from switching to injectable treatments. People who have difficulty swallowing, or who struggle with drug absorption or gastrointestinal issues, may benefit from switching from pills to injectables.

Some considerations

Adherence to an LAI depends on a person's willingness and ability to make it to their clinic appointments. People who visit their clinic once or twice yearly may find it inconvenient to come in six or 12 times a year. The importance of adherence can't be overstated. Not taking medication as required can lead to treatment failure and a rise in viral load. People who don't adhere to a regimen may also develop resistance to the drug types used in the treatment. That includes pills and injectables, but because injections are much less frequent the risk from non-adherence is minimized (though not eliminated).

If a person stops receiving injections and doesn't switch to another HIV treatment, drug resistance could develop. Fortunately, there is a little bit of flexibility (about one week before and one week after the scheduled injection, for CAB/RPV) for people who are late.

LAI for PrEP

Long-acting injectable cabotegravir (CAB-LA) can also be used for pre-exposure prophylaxis (PrEP), providing another HIV prevention option for people who prefer not taking tablets. Marketed as Apretude, CAB-LA can be used by adults and youth weighing at least 77 pounds as two initial injections that are given one month apart, and then every two months. Individuals can start with a lead-in of oral cabotegravir to see how well they tolerate the drug.

Like daily oral PrEP, CAB-LA does not protect against STIs. In fact, inside and outside of clinical trials, people taking CAB-LA have had high rates of new diagnoses of STIs including syphilis, chlamydia and gonorrhea. Such findings underscore the need for counseling and other sexual and reproductive health services when offering PrEP (either pills or CAB-LA). There is also the small, but significant, risk of developing drug resistance if someone acquires HIV very close to the time of initiating CAB-LA (and therefore still tests negative). Sophisticated (and expensive) diagnostics such as viral load testing could reduce this risk.

Which is better, oral PrEP or CAB-LA? They're both highly effective in preventing HIV when taken as prescribed. As with LAIs for treatment, the difference comes down to convenience and lifestyle. CAB-LA might help with adherence for people who find daily dosing with pills to be too difficult and would prefer longer-acting meds. The issue of privacy and having to hide medications (this is especially true for people who are unhoused) may make a long-acting injectable preferable for HIV prevention. But they'll have to make sure trips to the clinic are doable. On the other hand, some people just don't like getting injections, and for them an oral regimen works best.

The LAI pipeline

There is considerable research by companies trying to develop injectable treatments, whether they be intramuscular, subcutaneous, infusions, or implants, as well as pills that could be paired with LAIs.

Research is underway on:

Weekly islatravir combined with a six-monthly injection of lenacapavir, as well as trials of daily islatravir combined with other pills.

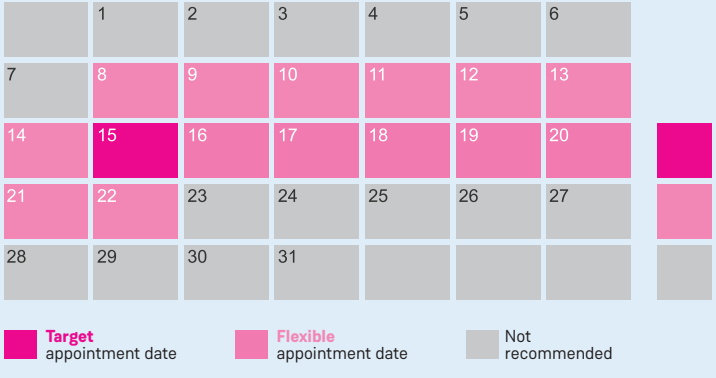
Broadly neutralizing antibodies (bNAbs) for HIV treatment, prevention and long-term viral remission. These include a phase II study pairing a bNAb infusion every two months with a monthly cabotegravir injection. Another trial pairs a bNAB given as an injection every two to four weeks with a fusion inhibitor (albuvirtide) given as a weekly injection. A phase II trial of injectable lenacapavir paired with bNAbs (given as infusions) every 6 months has shown promise.

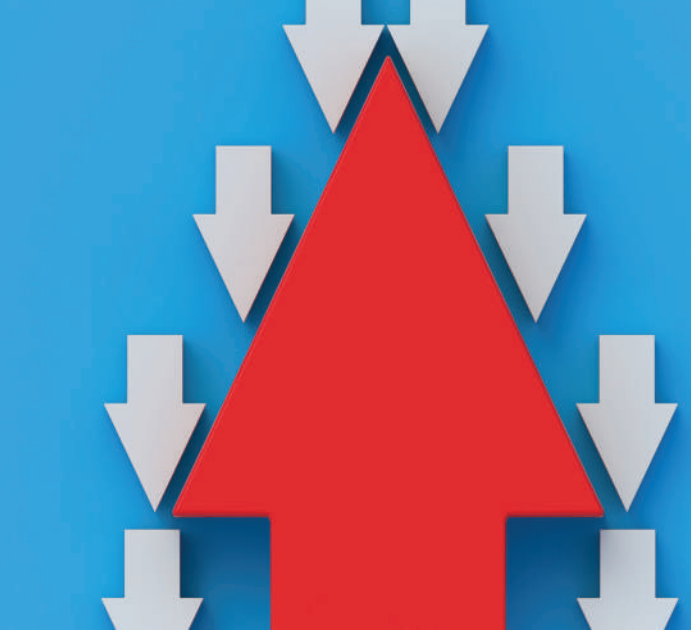
New medications in development include leronlimab (PRO 140, a CCR5 antagonist which could be given as a weekly injection) and UB-421 (a CD4 attachment inhibitor which could be given as an infusion every two weeks).

The importance of keeping scheduled appointment dates when you're taking a long-acting injectable medication

- Schedule an appointment date
- You have a window of flexibility from 7 days before to 7 days after your scheduled appointment date

Contact your healthcare provider if you can't make your scheduled appointment date. Make sure to set up a new appointment within your window of flexibility.





Resistance is not futile

There are more options than ever for people with multi-drug resistant HIV

BY **LARRY BUHL**

In February, the U.S. Food and Drug Administration (FDA) approved an expanded indication (usage) for Biktarvy to include people living with HIV (PLWH) with suppressed viral loads and resistance to M184V/I, one of the most common forms of drug resistance. According to manufacturer Giliead Sciences, the new indication makes Biktarvy (a three-drug combination of bictegravir, emtricitabine and tenofovir alafenamide) the first and only integrase strand transfer inhibitor (INSTI)-based regimen approved for PLWH whose virus has this mutation.

But it's not the only approved drug that can help PLWH with single- or multi-drug resistance (MDR), a serious condition where meds that should work simply don't. There are no clear data on how many people with HIV have MDR, which is defined as resistance to two or more drug classes and is more perilous than resistance to only one drug class. But according to Dr. Daniel Kuritzkes, professor of medicine at Harvard Medical School and chief of the Division of Infectious Diseases at Brigham and Women's Hospital, there is good news for this hard-to-treat population: the range of options for suppressing HIV has never been greater.

"What we are concerned about clinically is when people are resistant to numerous classes of drugs, where it becomes challenging to find an acceptable and effective regimen to establish viral resistance," Kuritzkes said. "That's less of an issue today, because therapy is better and we have more classes of drugs. In the late '90s and 2000s we did a lot of serial monotherapy when each new protease inhibitor [the first drug class of effective antiretroviral therapy] came out. But since the advent of integrase inhibitors and the second generation INSTIs—dolutegravir and bictegravir, along with boosted darunavir—there are small numbers of people for whom it's challenging to find a tolerable and effective regimen."

PLWH most likely to have MDR were on very early treatment that did not achieve complete viral suppression. As a result, they may have developed selective drug resistance to one or more regimens. People who acquired HIV at birth before effective therapies became available may also face MDR.

Kuritzkes said that in his practice in recent years he has seen only a handful of patients who truly meet the definition of MDR.

"In most cases we have found a regimen through these new generations like lenacapavir (LEN) and fostemsavir. There could be people resistant to at least one nucleoside and non-nucleoside and one PI but may be highly responsive to a regimen that includes a second-generation integrase inhibitor like dolutegravir or bictegravir and a boosted PI or other third agent." LEN is a capsid inhibitor and can be given as a shot every six months. It's highly effective because it's a novel drug class, so there should be no pre-existing resistance.

PLWH most likely to have MDR were on very early treatment that did not achieve complete viral suppression.

Kuritzkes added that physicians must also try to understand why a patient's regimen is failing, whether it's due to drug resistance, or if there is another explanation, such as lack of adherence or drug-drug interactions (other meds are interfering with the HIV drugs). A drug resistance test could confirm or rule out resistance, and asking the patient about adherence (and offering counseling if necessary) could provide more insight into a failing regimen.

More options for people with multi-drug resistant HIV

There is another HIV drug approved for PWH with MDR: ibalizumab (brand name Trogarzo), a monoclonal antibody given as an injection every other week, was approved in 2018. Beyond ibalizumab, fostemsavir (brand name Rukobia), an oral drug that binds to the HIV envelope and prevents virus entry, has been successful when paired with other meds.

In the future, PLWH with MDR may find new treatment options from broadly neutralizing antibodies (bNAbs) which can recognize and prevent a broad range of HIV strains from entering healthy cells. Gilead is studying LEN with a two bNAb combination, and presented phase two study findings at CROI last year. ViiV is looking at combining cabotegravir with bNAb combinations for treating virally-suppressed PLWH, and the company presented the most recent data at CROI 2024.

When combined with other drugs with higher barriers to resistance, like LEN or fostemsavir, there might be a role for bNAbs in those highly treatment experienced with MDR, Kuritzkes said

"I think we're several years from bNAbs being approved for use in treatment," he added, noting that the viral envelope that bNAbs target is highly variable and much larger than other proteins. "So it's harder to predict susceptibility or resistance based on genotype and therefore harder to sequence."

ISTOCK

HHS Guidelines for people starting HIV therapy for the first time

Regardless of CD4 count, 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. 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 clinicalinfo.hiv.gov for more information.

Recommended initial regimens for most people with HIV without a history of CAB-LA

INSTI + two NRTIs

Biktarvy (A1)

Triumeq (A1)
*If HLA-B*5701 negative*

Tivicay + **Descovy** or **Truvada**[a] (A1)

INSTI + one NRTI

Dovato (A1)
Except for individuals with HIV RNA greater than 500,000 copies/mL, HBV coinfection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available

Recommended initial regimen for people with a history of CAB-LA

Boosted darunavir + two NRTIs

INSTI genotypic resistance testing should be done before the start of ART. If treatment is begun prior to results of genotypic testing, the following regimen is recommended until genotype results are available:

Symtuza (A3)

Prezcobix + **Descovy** or **Truvada**[a] (A3)

Boosted Prezista + **Descovy** or **Truvada**[a] (A3)

RATING OF RECOMMENDATIONS

A: Strong
B: Moderate
C: Weak

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.

Recommended initial regimens in certain clinical situations

KEY TO ABBREVIATIONS

CD4: CD4 T lymphocyte, "T cell"
HIV RNA: viral load
INSTI: integrase strand transfer inhibitor
NNRTI: non-nucleoside reverse transcriptase inhibitor
NRTI: nucleoside reverse transcriptase inhibitor
PI: protease inhibitor

INSTI + two NRTIs

Stribild (B1)[b]

Genvoya (B1)[b]

Isentress + **Descovy** (B2) or **Truvada** (B1)

Isentress HD + **Descovy** (B2) or **Truvada** (B1)

Boosted PI + two NRTIs

In general, Prezcobix or boosted Prezista is preferred over Evotaz or boosted Reyataz

Symtuza (B1)

Prezcobix[a] + **Descovy** or **Truvada**[a] (A1) or **Epzicom** (B2) (If HLA-B*5701 negative)

Boosted Prezista + **Descovy** or **Truvada**[a] (A1) or **Epzicom** (B2) (If HLA-B*5701 negative)

Evotaz + **Descovy** or **Truvada**[a] (B1)

Boosted Reyataz + **Descovy** or **Truvada**[a] (B1)

NNRTI + two NRTIs

Delstrigo (B1)

Pifeltro + **Descovy** (B3)

Atripla (B1)

Symfi (B1)

Symfi Lo (B1)

Sustiva + **Descovy** (B2)

Complera (B1) or **Odefsey** (B2)
If HIV RNA less than 100,000 copies/mL and CD4 count greater than 200 cells/mm^3

Regimens to consider when NRTI backbones containing abacavir, tenofovir alafenamide, and tenofovir disoproxil fumarate cannot be used or are not optimal

Dovato (A1)
except for individuals with HIV RNA greater than 500,000 copies/mL, HBV coinfection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available

Boosted Prezista + **Isentress** (twice daily) (C1)
if HIV RNA less than 100,000 copies/mL and CD4 count greater than 200 cells/mm^3

Boosted Prezista once daily + **lamivudine** (C1)

FOOTNOTES
[a] Or generic equivilant.
[b] COBI should be avoided in pregnancy because lower concentrations of COBI and its boosted drugs—EVG, DRV, and ATV—have been observed during the second and third trimesters. For individuals with viral suppression who become pregnant while on a COBI-containing regimen and wish to remain on that regimen after counseling regarding lower drug concentration, frequent viral load monitoring is recommended. For further information, refer to the Perinatal Guidelines (clinicalinfo.hiv.gov).

GENERIC REGIMENS OR COMPONENTS AVAILABLE
(SEE "CLASS LIST" ON PAGE 25)

3TC
ABC
ATV (Reyataz)
EFV
EFV/TDF/FTC
EFV/TDF/3TC
ETR
FTC
RTV (Norvir)
TDF
TDF/FTC

The U.S. Department of Health and Human Services (HHS) produces several sets of clinical guidelines for HIV care:

- Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV
- Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV
- Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection
- Guidelines for the Prevention and Treatment of Opportunistic Infections in Children with and Exposed to HIV
- Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States

HHS also provides two sets of clinical guidance in HIV:

- Guidance for Non-HIV-Specialized Providers Caring for Persons with HIV Who Have Been Displaced by Disasters (Such as a Hurricane)
- Guidance for COVID-19 and People with HIV

In addition, guideline reports from the U.S. Centers for Disease Control and Prevention (CDC) are provided on the following topics:

- Pre-exposure prophylaxis (PrEP)
- Occupational post-exposure prophylaxis (PEP)
- Non-occupational post-exposure prophylaxis (nPEP)

GO TO clinicalinfo.nih.gov.

A guide to the Drug Guide

Plus, a few things to know about HIV treatment

BY **JEFF BERRY** AND **ENID VÁZQUEZ**

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

The scientific evidence for HIV treatment is so strong that HHS recommends starting therapy on the same day an HIV diagnosis is received.

Treatment helps keep people healthy and keeps AIDS at bay, among other benefits. It can even prevent the transmission of HIV to sex partners.

All HIV medications are listed in alphabetical order on page 25.

Many of the drugs on the list are rarely used by themselves because they are instead taken as part of a co-formulation with other meds. For example, Emtriva is usually used by way of Descovy or Biktarvy. Descovy itself (two drugs in one pill) is usually used by way of a single-tablet regimen (STR). Biktarvy is an STR.

What does HIV treatment do?

The goal of therapy is to suppress the amount of virus (called "viral load") to an undetectable level. This means that the amount of virus in your blood is so low, it cannot be detected by viral load tests. Undetectable viral load (usually considered less than 50 copies per milliliter of blood) will help keep you healthy; 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. HIV treatment should also raise the number of your CD4+ T cells, a measure of the immune system.

Tests to take before starting HIV therapy

People should be tested for STIs, hepatitis B and C virus, and HIV drug resistance. These conditions and their treatment may affect the HIV medications that can be taken.

Rapid Start

Going on treatment when receiving an HIV diagnosis is called "rapid start" or "rapid ART." "ART" stands for "antiretroviral therapy" (since HIV is a

ISTOCK

retrovirus). Rapid ART is also known as "same-day ART" and "treatment upon diagnosis."

With the rapid ART strategy recommended by HHS, treatment can begin while awaiting test results.

Only four HIV medications qualify for use as rapid ART under HHS and IAS-USA guidelines. They are:

1. Biktarvy
2. Dovato
3. Tivicay + TAF or TDF + FTC or 3TC (basically, Tivicay plus Descovy or Truvada)
4. People living with HIV who have used Apretude (for PrEP) should use boosted darunavir (Prezista or Prezcobix) + TAF or TDF + FTC or 3TC for rapid start. Symtuza alone meets those requirements.

What does HIV treatment consist of?

HIV therapy is made up of medications from at least two drug classes. HIV drugs are called "antiretrovirals" (ARVs).

A single-tablet regimen (STR) consists of two or more ARVs from at least two drug classes, and form a complete HIV treatment taken by itself.

Cabenuva is a complete regimen that is given as two long-acting injections every two months (or monthly).

A fixed-dose combination (FDC) combines two or more ARVs in one pill but is not a complete regimen.

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.

Medications that are approved by the U.S. Food and Drug Administration (FDA) for highly treatment-experienced individuals (and recommended as such by HHS) include Rukobia, Selzentry, Sunlenca and Trogarzo. Prezista and Prezcobix are also frequently used as part of that mix.

Treatment-experienced individuals may need to switch therapy due to side effects or drug resistance. Some treatment-experienced people, however, do well with medications that are easier to take, such as Biktarvy or Juluca, both of which are STRs.

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

What is drug resistance?

If treatment is not taken correctly or is unable to completely suppress the virus, it might mutate (make changes in its viral genetic structure). This can make therapy less effective or even ineffective. This drug resistance occurs mostly through missed doses. Fortunately, many of the widely used HIV drugs today have a high barrier to resistance, are easier to take, and have few if any side effects. However, it is better to avoid missing doses. Drug resistance may lead to the need for more complicated therapy (such as more pills).

Drug names

Medications generally have three names. For example, Epivir is a brand name, lamivudine is the generic name and 3TC is the shortened form of its chemical name.

Taking HIV treatment

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.

IRIS

Individuals with a weak immune system who go on HIV therapy may develop something called IRIS, which stands for "immune reconstitution inflammatory syndrome." It is rarely seen now thanks to people starting treatment as soon as possible when diagnosed, which helps the immune system stay healthy. IRIS was generally seen with less than 100 T cells and a history of AIDS-defining opportunistic infections (OIs). Notify your doctor right away of any symptoms so that you can be treated as needed. IRIS is a sign that the immune system is actually getting stronger.

Checking in with your providers

You can play an active role in your health care by talking to your doctor, nurse practitioner or other provider. Clear and honest communication can help you both make smart choices about your health. It's important to be honest and up-front about your symptoms even if you feel embarrassed or shy. Have an open dialogue—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. Each person is different; you and your health care provider can decide which drugs to use.

Here are a few tips that can help you talk with your provider 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 provider 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 provider's contact information and their preferred method of communication.
- Remember that nurses and pharmacists are also good sources of information.

Pricing

As one HIV specialty pharmacist likes to say, drug pricing is like the sticker price on a car. Much of it depends on the negotiation.

The Average Wholesale Price (AWP) on each drug page is a way to compare the cost of drugs. It is not what you would pay if you were to pay the full retail price. (That's why AWP's commonly referred to as "ain't what's paid.")

In her comments on the drug pages, Dr. Melanie Thompson refers to the Wholesale Acquisition Cost (WAC).

The AWP is "an estimate of the price retail pharmacies pay for drugs from their wholesale distributor." WAC is "an estimate of the manufacturer's list price for a drug to wholesalers or other direct purchasers, not including discounts or rebates. This price is defined by federal law."

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.

More information online

U.S. Dept. of Health and Human Services HIV treatment guidelines
clinicalinfo.hiv.gov

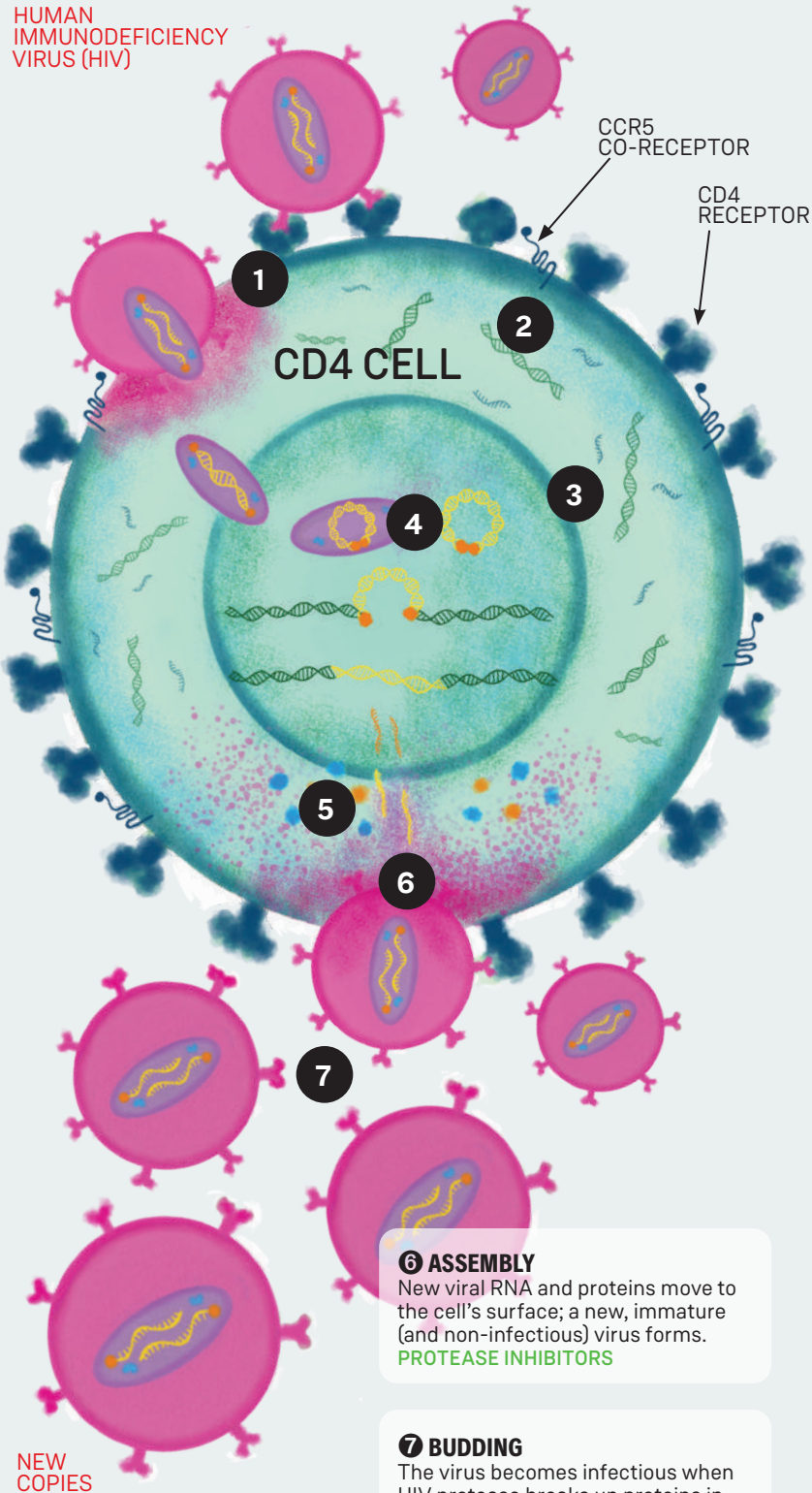
HIV treatment guidelines from the International Antiviral Society-USA
iasusa.org/resources/guidelines

University of Liverpool HIV drug interactions calculator
hiv-druginteractions.org

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

❸ REVERSE TRANSCRIPTION
Viral DNA is formed by reverse transcription.
NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NRTIs, or "nukes") and NUCLEOSIDE REVERSE TRANSCRIPTASE TRANSLOCATION INHIBITORS (NRTTIs, also "nukes"), including these in development:
- **islatravir**

NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NNRTIs, or "non-nukes")

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

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

❻ ASSEMBLY
New viral RNA and proteins move to the cell's surface; a new, immature (and non-infectious) virus forms.
PROTEASE INHIBITORS

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

MATURATION INHIBITOR

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

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)
- **LAI** — 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
30	**Atripla**	STR	efavirenz/emtricitabine/tenofovir DF (EFV/FTC/TDF)
26	**Biktarvy**	STR	bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF)
35	**Cabenuva**	LA	cabotegravir/rilpivirine long-acting (CAB-LA/RPV-LA) injectable
51	**Cimduo**	NRTI *	lamivudine/tenofovir DF (3TC/TDF)
33	**Complera**	STR	rilpivirine/emtricitabine/tenofovir DF (RPV/FTC/TDF)
31	**Delstrigo**	STR	doravirine/lamivudine/tenofovir DF (DOR/3TC/TDF)
48	**Descovy**	NRTI *	emtricitabine/tenofovir alafenamide (FTC/TAF)
27	**Dovato**	STR	dolutegravir/lamivudine (DTG/3TC)
45	**Edurant**	NNRTI	rilpivirine (RPV)
50	**Emtriva**	NRTI	emtricitabine (FTC)
50	**Epivir**	NRTI	lamivudine (3TC)
49	**Epzicom**	NRTI *	abacavir/lamivudine (ABC/3TC)
43	**Evotaz**	PI / PKE	atazanavir/cobicistat (ATV/COBI)
32	**Genvoya**	STR	elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (EVG/COBI/FTC/TAF)
44	**Intelence**	NNRTI	etravirine (ETR)
41	**Isentress HD**	INSTI	raltegravir (RAL)
29	**Juluca**	STR	dolutegravir/rilpivirine (DTG/RPV)
52	**Norvir**	PKE	ritonavir (RTV)
33	**Odefsey**	STR	rilpivirine/emtricitabine/tenofovir alafenamide (RPV/FTC/TAF)
46	**Pifeltro**	NNRTI	doravirine (DOR)
42	**Prezcobix**	PI / PKE	darunavir/cobicistat (DRV/COBI)
42	**Prezista**	PI	darunavir (DRV)
43	**Reyataz**	PI	atazanavir sulfate (ATV)
37	**Rukobia**	AI	fostemsavir (FTR)
38	**Selzentry**	EI	maraviroc (MVC)
32	**Stribild**	STR	elvitegravir/cobicistat/emtricitabine/tenofovir DF (EVG/COBI/FTC/TDF)
36	**Sunlenca**	CAI	lenacapavir (LEN)
47	**Sustiva**	NNRTI	efavirenz (EFV)
30	**Symfi/Symfi Lo**	STR	efavirenz/lamivudine/tenofovir DF (EFV//3TC/TDF)
34	**Symtuza**	STR	darunavir/cobicistat/emtricitabine/tenofovir alafenamide (DRV/COBI/FTC/TAF)
40	**Tivicay**	INSTI	dolutegravir (DTG)
28	**Triumeq**	STR	dolutegravir/abacavir/lamivudine (DTG/ABC/3TC)
39	**Trogarzo**	EI	ibalizumab-uiyk (IBA)
51	**Truvada**	NRTI *	emtricitabine/tenofovir DF (FTC/TDF)
53	**Tybost**	PKE	cobicistat (COBI)
51	**Viread**	NRTI	tenofovir disoproxil fumarate (tenofovir DF, or TDF)
49	**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

50 mg bictegravir, 200 mg emtricitabine, 25 mg tenofovir AF
BIC (INSTI)/FTC and TAF (two NRTIs)

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

★ Recommended initial regimen for most people with no history of Apretude (CAB-LA) for PrEP

➤ **Recommended for rapid ART** for someone newly diagnosed or entering care with no or minimal labs available.

STANDARD DOSE

One tablet once daily, with or without food, for people taking HIV treatment for the first time (treatment-naïve) or individuals with suppressed viral load on a stable HIV regimen who have no history of treatment failure. Consideration may also be given to using Biktarvy (or other second-generation integrase inhibitors like Tivicay plus 2 NRTIs) for individuals with previous virologic failure (assuming no INSTI resistance and at least one of the NRTIs is fully active).

For adults and children weighing at least 55 pounds (25 kg), use standard dose above or see package labeling. A pediatric formulation is available for children at least 2 years old and weighing 30.8–55 pounds (14–25 kg), Biktarvy Low Dose, contains BIC 30 mg/FTC 120 mg/TAF 15 mg; it is taken as one tablet daily, with or without food.

Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. 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 (although rarely experienced) include headache, nausea, and diarrhea. Data associate INSTIs and TAF 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. HHS 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 carbamazepine, eslicarbazepine, oxcarbazepine, phenobarbital, phenytoin, rifabutin, rifampin, rifapentine and 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

Biktarvy is widely prescribed because of its favorable efficacy, safety, tolerability and drug resistance profile. The FDA granted approval in February for Biktary use by individuals with NRTI drug resistance. Five-year data released in 2022 show 98% undetectable viral load rate in more than 1,000 individuals from Studies 1489 and 1490, with no development of drug resistance, in the open-label extension (OLE) at Weeks 144–240. Data had accumulated showing that Biktarvy works for people who have detectable virus when they switch to it from another regimen (having experienced virologic failure on their previous regimen). However, people who have previously experienced virologic failure when using another integrase inhibitor, such as Isentress or Tivicay, may be prone to losing virologic control after switching to Biktarvy. Biktarvy is a preferred drug regimen for PEP (post-exposure prophylaxis—preventing HIV acquisition after a potential exposure), as well as two other regimens: Tivicay along with Truvada or Descovy or Isentress HD with Truvada or Descovy. Biktarvy is now an alternative initial regimen in pregnancy (see page 10). Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

DR. MELANIE THOMPSON: Unless previously on long-acting cabotegravir (Apretude) as PrEP, Biktarvy is recommended for initial therapy, including for "rapid" or "same-day" start of HIV treatment. Based on accumulating safety data, Biktarvy was recently upgraded to an "alternate" treatment in pregnancy by the HHS perinatal antiretroviral guidelines. Studies suggest that people with suppressed virus (who are undetectable) on dolutegravir (Tivicay) + TDF/FTC (Truvada), TDF/3TC or TAF/FTC (Descovy) may safely switch to Biktarvy, even in the presence of a past M184V mutation.

Dofetilide, a medication for heart arrhythmia, cannot be co-administered because serious heart rhythm disturbances could occur. Some medicines for seizures or tuberculosis and St. John's wort also cannot be taken with Biktarvy. Biktarvy increases metformin levels, so talk with your HIV clinician if you are on this drug when starting Biktarvy. Importantly, supplements containing aluminum, magnesium, calcium, zinc, or iron can decrease bictegravir levels and are a common source of blips or persistent low-level viremia. Biktarvy should be taken 2 hours before or 6 hours after aluminum, magnesium, zinc, calcium or iron supplements, although calcium and iron may be taken at the same time as Biktarvy if taken with a meal. It's also very important to know that Biktarvy contains TAF, which treats hepatitis B (HBV), and that stopping Biktarvy without continuing a drug with activity against HBV can result in a hepatitis flair that could be serious. Pay attention to this especially if switching to a two-drug regimen like Dovato, Juluca, or Cabenuva.

Several studies have shown weight gain in some people who are beginning INSTIs, especially dolutegravir or bictegravir, but the mechanism and clinical significance are not yet clear. Concern about weight gain should not be a reason to avoid INSTIs because of their substantial benefits. The association of TAF with weight gain appears to be modest and is still being studied. It's important to watch your diet and stay physically active regardless of what you are taking. All INSTIs have the potential for insomnia or, rarely, worsening of depression or suicidal ideation, particularly if there are pre-existing mental health issues. Within weeks of starting bictegravir, the blood creatinine level is expected to rise by about 0.1 mg/dL because BIC blocks creatinine secretion in the kidney. The effect persists and remains steady as long as bictegravir is taken, but it is important to recognize that this is not because of kidney toxicity.

ACTIVIST JOEY WYNN: Biktarvy is still the current king of the hill, a relatively small, once-a-day pill with an entire regimen in it. This is one of the best options for people who are okay with taking pills daily, and is ideal for people just starting their first regimen. Pricing can be a concern in some scenarios, but many resources are available to help defray or remove costs entirely based on your situation. Biktarvy definitely has the lion's share of the field for now, with relatively few side effects and is easily tolerated.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$4,554.29/month

Dovato

50 mg dolutegravir, 300 mg lamivudine
DTG (INSTI), 3TC (NRTI)

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

★ HHS 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, with no history of Apretude (CAB-LA) for PrEP

➤ **Recommended for rapid ART** for someone newly diagnosed or entering care with no or minimal labs available.

STANDARD DOSE

One tablet once daily, with or without food, for treatment-naïve people who have no known resistance to components of the regimen: dolutegravir and lamivudine. Dovato is now available in blister packs.

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 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. HHS 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 or the antiarrhythmic dofetilide (a heart medication). 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. Do not take with oxcarbazepine, eslicarbazepine, phenytoin, or phenobarbital. Dovato should be taken two hours before or six hours after taking laxatives or antacids, the ulcer medication sucralfate, oral iron or calcium supplements/vitamins, or buffered medications. It can be taken with iron- or calcium-containing supplements/vitamins 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 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

Basically, this medicine is Triumeq without the abacavir component (brand name Ziagen, also found in Epzicom). Dovato is now available in a blister pack option (on foil-backed sheets instead of in a bottle). 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 + 3TC was found to be non-inferior to the triple drug regimen of DTG + Truvada (emtricitabine and tenofovir DF combined in one pill). 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 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 a preferred medication during pregnancy as well as for people who are trying to conceive, U.S. HIV perinatal treatment guidelines suggest using three-drug regimens for these individuals. Find the discussion on page C-55 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: Dovato is the only two-drug regimen recommended for initial therapy, although it has some limitations. Dovato does not treat hepatitis B, so it should not be taken by people with hepatitis B (HBV) unless a drug such as entecavir that is active against HBV is also given. In most cases, people with HBV should begin a regimen containing tenofovir (TAF or TDF) and 3TC or FTC. Also, Dovato should not be the initial choice of therapy if the viral load is above 500,000 copies/mL. In addition, resistance testing should be conducted before starting Dovato for initial therapy because 3TC resistance is sometimes transmitted and could compromise the effectiveness of Dovato. Dovato, therefore, is not recommended for "rapid" or "same day" start before lab results are available. Before starting Dovato, resistance testing, hepatitis B serology, and viral load should be conducted to guide choice of therapy. As with other INSTI-containing regimens, Dovato should not be used as initial therapy for people who acquired HIV after taking Apretude unless an INSTI genotype is available and shows sensitivity to dolutegravir. People with suppressed virus on a TAF-based regimen who have never experienced prior treatment failure and who don't have hepatitis B may safely switch to Dovato. Possible INSTI side effects like insomnia and new or worsening depression also apply to Dovato. Drug interactions of note include an increase in the levels of dofetilide (which is contraindicated), metformin, and some other drugs when taken with dolutegravir. Talk with your clinician if you are taking metformin when you begin Dovato. Dolutegravir levels decrease with some seizure or tuberculosis medicines and St. John's wort. Managing drug interactions is tricky, so be sure any clinician who is prescribing drugs for you knows all of the medicines you are taking, including over-the-counter drugs and supplements. Dolutegravir increases serum creatinine by 0.1-0.15 mg/dL within a few weeks of beginning therapy, but this is due to inhibition of creatinine secretion in the kidney rather than true kidney toxicity. As with all INSTIs, Dovato should be taken 2 hours before or 6 hours after aluminum, magnesium, zinc, calcium or iron supplements, although calcium and iron may be taken at the same time as Dovato if taken with a meal.

The price of Dovato is higher than the price of Tivicay alone, representing quite an inflated price for a month of generic 3TC whose wholesale acquisition cost is as low as $75/month.

ACTIVIST JOEY WYNN: Some folks are looking to take fewer medications; a two-drug combo could be for you if that is your priority. This combo is still a hard "no" for anyone on metformin for diabetes or on a tuberculosis (TB) therapy, unless you take an extra dolutegravir pill to compensate for the interaction. Overall, this is a good choice, and very underrated; talk to your provider to see if this is right for you, especially if you want to reduce the number of medications you take daily.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$3,371.68/month

Triumeq

50 mg dolutegravir, 600 mg abacavir, 300 mg lamivudine
DTG, (INSTI); ABC, 3TC (two NRTIs)

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

★ Recommended initial regimen for most people if HLA-B*5701 negative with no history of Apretude (CAB-LA) for PrEP

STANDARD DOSE

One tablet once daily, with or without food, for people with no evidence of INSTI resistance. An additional 50 mg dose of dolutegravir (brand name Tivicay) separated by 12 hours from Triumeq is required for people who have INSTI drug resistance or are taking certain other medications.

For adults and children. Triumeq PD, which are tablets that are dissolved in 20 ml of water and taken within 30 minutes of mixing, are for pediatric patients 22–55 pounds (10–25 kg). Triumeq PD is not interchangeable with the adult formulation. Therefore, adults should not take the pediatric formulation. 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. If an alternative dosage form is required, may consider using individual components available in other formulations.

➤ 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 in 2021 did not observe the weight gain observed 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. HHS 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; see warning card that comes with Triumeq. 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 the antiarrhythmic dofetilide (a heart medication). 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 eslicarbamazepine, 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, rifampin, Sustiva, or Rukobia or Aptivus + Norvir, take an additional dose of dolutegravir (Tivicay) 12 hours after taking Triumeq dose. The additional dose of dolutegravir is based on the individual's weight. 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. Triumeq, as well as its individual components, is recommended as a preferred initial regimen in pregnancy. 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

$4,244.88/month

DR. MELANIE THOMPSON:

Abacavir, which is a component of Triumeq, has fallen out of favor for initial therapy. Abacavir hypersensitivity can be life-threatening, although its incidence is greatly reduced by HLA-B*5701 genetic testing. A negative test result is needed before prescribing regimens containing abacavir; therefore, Triumeq cannot be used for "rapid" or "same day" start, before labs are available. There also are longstanding concerns that abacavir may increase the risk of cardiovascular disease.

Triumeq shares side effects common to all INSTIs, including insomnia or, rarely, worsening of depression or suicidal ideation, particularly if there are pre-existing mental health issues. Dolutegravir has been associated with weight gain, so keep track of your weight and pay attention to diet and exercise if you are starting Triumeq. Dolutegravir also slightly raises the level of creatinine in the blood by 0.1-0.15 mg/dL by blocking its secretion at the kidney, not by causing kidney damage.

Drug interactions with dolutegravir are few but some are important. Do not take dofetilide or St. John's wort; talk with your HIV care provider if you are taking metformin or medications for seizures or tuberculosis. As with all INSTIs, Triumeq should be taken 2 hours before or 6 hours after aluminum, magnesium, zinc, calcium, or iron supplements, although calcium and iron can be taken with Triumeq if taken with a meal. For more info on drug interactions, see the comments about Tivicay.

ACTIVIST JOEY WYNN:

The size of the pill alone poses a big challenge, especially for someone not comfortable with taking pills in the first place. This option has a number of drug-drug interactions that make it a second-line choice, based on the ease of other options. People with hepatitis B should definitely pass on this option. Probably not a first line choice if you're just starting out on pills.

Juluca

50 mg dolutegravir, 25 mg rilpivirine
DTG (INSTI), RPV (NNRTI)

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

✔ Recommended as continuation therapy for people with undetectable HIV viral load for at least 6 months

STANDARD DOSE

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

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. HHS 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 a 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, eslicarbamazepine, oxcarbazepine, phenobarbital, and phenytoin) or St. John's wort. HHS HIV treatment guidelines suggest 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 one of the smallest STRs, 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-55 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; juluca.com;
(877) 844-8872

AVERAGE WHOLESALE PRICE

$3,978.37/month

DR. MELANIE THOMPSON: Juluca is not approved for initial therapy but is used for maintenance of viral suppression in people whose virus has been suppressed on their current regimen for at least 6 months. If you have hepatitis B, you must take another hepatitis B-active drug if you take Juluca, as neither of its components has activity against HBV. There are a number of drug interactions with Juluca (see drug interactions listed under Tivicay.) Juluca should be taken with a meal for best absorption of rilpivirine.

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. A creatinine increase of about 0.1 mg/dL should be expected and is due to dolutegravir's effect blocking kidney secretion of creatinine rather than kidney toxicity. (For further information about dolutegravir and rilpivirine, see Tivicay and Edurant.)

Because of similarities between cabotegravir and dolutegravir, some have suggested that Juluca might be used as a bridging drug if doses of Cabenuva cannot be given on time. This seems reasonable but has not been studied in clinical trials.

ACTIVIST JOEY WYNN: Juluca was the first two-drug pill; seven years later, I believe the benefits do not outweigh the difficulties of this option. Many drug-drug interactions and numerous reports of diarrhea and headaches make this a difficult choice in today's market. The timing of taking this with other pills such as vitamins and other over-the-counter products make this a complicated regimen to manage. I do not know of anyone still on this option; but I'm sure for a small handful of folks it works and they don't want to switch. For people about to select a new therapy, this probably isn't a good option to begin your journey, so keep looking.

Atripla

600 mg efavirenz, 200 mg emtricitabine, 300 mg tenofovir DF
EFV (NNRTI), FTC and TDF (two NRTIs)

■ Generic is available

Symfi

600 mg efavirenz, 300 mg lamivudine, 300 mg tenofovir DF
EFV (NNRTI), 3TC and TDF (two NRTIs)

Symfi Lo

400 mg efavirenz, 300 mg lamivudine, 300 mg tenofovir DF
EFV (NNRTI), 3TC and TDF (two NRTIs)

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

✔ Other complete HIV regimens; HHS recommended initial therapy in certain clinical situations

STANDARD DOSE

One tablet once daily on an empty stomach, preferably at bedtime.

Atripla is for adults and children 12 years of age and older weighing at least 88 pounds (40 kg). Symfi Lo is for adults and pediatric patients weighing at least 77 pounds (35 kg) and Symfi is for those who are 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. Should not be used in people with moderate or severe kidney or liver impairment.

➤ **SEE THE INDIVIDUAL DRUGS CONTAINED IN ATRIPLA:** Sustiva and Truvada.

➤ **SEE THE INDIVIDUAL DRUGS CONTAINED IN SYMFI AND SYMFI LO:** Sustiva, Epivir, 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. People should be screened for depression and suicidality. Dizziness, drowsiness, abnormal or vivid dreams, difficulty concentrating, rash, diarrhea, nausea, fatigue, headache, or insomnia may go away after a few weeks. TDF is associated with long-term decreases in bone mineral density. Prior to initiation, kidney function and hepatitis B status should be assessed (monitor liver enzymes closely in people with 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. Late-onset neurotoxicity, including ataxia and encephalopathy (impaired consciousness, confusion, psychomotor slowing, psychosis and delirium), may occur months to years after beginning EFV. A link between efavirenz and birth defects in humans has not been supported in meta-analyses. The recommendation is that pregnant people 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). It is recommended to screen for antenatal and postpartum depression in recently pregnant people. Efavirenz can cause a false positive result for marijuana on certain drug tests. A confirmatory test can be done.

POTENTIAL DRUG INTERACTIONS

Avoid taking with drugs that negatively affect the kidneys, including chronic use or high doses of anti-inflammatory drugs for pain such as aspirin, ibuprofen and naproxen. Should not be taken with voriconazole, ergot derivatives, midazolam, pimozide, triazolam, bepridil or St. John's wort, or medications that prolong QTc interval (these abnormal heart rhythms can make the heart stop) or with a risk for torsades de pointes. It is recommended to add 200 mg Sustiva (800 mg total) when taking rifampin for people weighing at least 110 pounds. 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 considered. Effectiveness of birth control pills may be decreased. Closer monitoring and dose adjustments may be required with posaconazole (avoid unless benefit outweighs potential risk) and itraconazole. Monitor clarithromycin effectiveness or consider azithromycin. Monitor immunosuppressant level 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. Use caution with Harvoni; monitor renal function closely. 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 not listed here.

MORE INFORMATION

Check with your provider or pharmacist first before stopping these drugs, so that you avoid the rapid development of HIV resistance to efavirenz. A genetic trait affecting efavirenz metabolism, causing a higher rate of side effects, occurs more in African Americans. NNRTIs are not recommended for HIV-2, usually found outside the U.S., as it is resistant to NNRTIs. If you can't sleep, ask your doctor about gradually adjusting the timing of your dose until it's taken during the day. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

MANUFACTURERS

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

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

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

AVERAGE WHOLESALE PRICE

Atripla: **$3,593.66**/month
Generic is available.

Symfi: **$2,201.46**/month
Symfi Lo: **$2,201.46**/month

DR. MELANIE THOMPSON:

Atripla, the first once-daily complete HIV regimen, has not been recommended for initial therapy in the U.S. for a number of years, largely due to the many side effects associated with efavirenz. 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. Efavirenz-containing generics Symfi and Symfi Lo both use 3TC instead of FTC. Symfi Lo contains only 400 mg of efavirenz and may have fewer side effects. The IMPAACT 2010 study found that infants exposed to efavirenz in pregnancy were more likely to experience growth stunting than those exposed to dolutegravir. In 2024, there is really no reason to prescribe these drugs, unless someone is doing well on them and is unwilling to change to more modern regimens.

ACTIVIST JOEY WYNN:

The gold standard for many years, Atripla fell out of favor due to central nervous system side effects and a problematic resistance profile (as well as a host of other complications and contraindications). I'm not sure why anyone would get on this treatment as a new start, but there is still a small minority of folks staying on it until they have a reason to start shopping for a new combination. Symfi and Symfi Lo are "branded generic" versions of Atripla. Same kinds of issues apply, although the greatly reduced cost gives these options a minor role in some limited "budget-constrained" markets; but still definitely not on a first-line selection by any means.

Delstrigo

100 mg doravirine, 300 mg lamivudine, 300 mg tenofovir DF
DOR (NNRTI), 3TC and TDF (two NRTIs)

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

✔ Other complete HIV regimen; HHS recommended initial therapy in certain clinical situations

STANDARD DOSE

One tablet once daily, with or without food, for adults and pediatric patients weighing at least 77 pounds (35 kg) 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.

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 (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 (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 taking Pifeltro 100 mg tablet approximately 12 hours after Delstrigo. 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

Standalone 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 HHS guidelines, "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 approved for initial therapy, based on clinical trials comparing it to efavirenz or ritonavir-boosted darunavir, but it is not recommended for initial therapy in most people with HIV in the U.S. because it has never been compared directly to an INSTI-containing regimen. (The European guidelines, however, have elevated Delstrigo to be used in initial therapy.) Doravirine had fewer neuropsychiatric side effects than efavirenz in the DRIVE-AHEAD trial, and less diarrhea and nausea than ritonavir-boosted darunavir in 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) was more than with efavirenz (0.6 kg) and similar to ritonavir-boosted darunavir (1.4 kg) at 48 weeks, but all were similar at week 96. Delstrigo is not recommended in pregnancy due to insufficient data on doravirine.

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 hopes that doravirine might be genetically more robust and less likely to select for drug resistance, however, have been met with disappointment. With two generic drugs, you would expect Delstrigo's average wholesale cost to be lower than it is.

ACTIVIST JOEY WYNN: This is one of the first viable older combinations in a "new generic formulation." Pricing is great, but an older regimen with a few negatives makes this a second-line option. I believe doravirine has a better resistance profile than others in the NNRTI class, as well as an attractive lipid profile; in light of this it could be an option for people concerned about cardiovascular issues.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$2,552.40/month

Genvoya

150 mg elvitegravir, 150 mg cobicistat, 200 mg emtricitabine, 10 mg tenofovir AF
EVG (INSTI), COBI (PK booster), FTC and TAF (two NRTIs)

Stribild

150 mg elvitegravir, 150 mg cobicistat, 200 mg emtricitabine, 300 mg tenofovir DF
EVG (INSTI), COBI (PK booster), FTC and TDF (two NRTIs)

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

✔ Recommended initial regimen in certain clinical situations and there is no history of Apretude (CAB-LA) for PrEP

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.

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. Use is not recommended in people with severe liver problems.

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. HHS 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 all for the treatment of hepatitis B, as the emtricitabine and tenofovir components already treat HBV. 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. No significant interactions with beclomethasone or prednisolone. Use caution with beta blockers and calcium channel blockers. 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. Take lower dose of colchicine. 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.

DR. MELANIE THOMPSON: These STRs differ only in the presence of TAF (Genvoya) or TDF (Stribild), but neither is recommended for initial therapy for most people because elvitegravir requires a cobicistat booster, introducing many drug-drug interactions, and because of elvitegravir's genetic fragility compared to dolutegravir and bictegravir. When taken together, TDF and COBI sometimes have been associated with kidney toxicity and low bone density, so close monitoring is important. These drugs should not be used in pregnancy due to the risk of inadequate drug levels associated with cobicistat in the second and third trimesters.

ACTIVIST JOEY WYNN: Gilead's strategy to revise and update the Stribild combo by switching out the TDF with TAF to make Genvoya enabled them to continue its market domination. It's a shrewd strategy that has worked for years, but at this point, no one should be on a boosted therapy, unless you have discussed it with your provider and there are no better options for you.

Stribild: Co-administer bosentan and immunosuppressants such as Prograf, Gengraf, Neoral, and Sandimmune with caution. Taking with Harvoni, Olysio, Viekira Pak, or Zepatier is not recommended. Monitor kidney function more closely with Epclusa.

MORE INFORMATION

Switching regimens should be considered for anyone who is pregnant, especially during the third trimester, due to lower drug levels. 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

$4,554.29/month

STRIBILD AWP

$4,777.46/month

Odefsey

25 mg rilpivirine, 200 mg emtricitabine, 25 mg tenofovir AF
RPV (NNRTI), FTC and TAF (two NRTIs)

Complera

25 mg rilpivirine, 200 mg emtricitabine, 300 mg tenofovir DF
RPV (NNRTI), FTC and TDF (two NRTIs)

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

✔ Recommended initial regimen in certain clinical situations if viral load <100,000 copies/mL and CD4 count >200/mm³

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.

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

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

According to DHHS guidelines, people taking HIV treatment for the first time should have an HIV RNA (viral load) of less than 100,000 copies/mL and CD4 T cell count must be above 200 cells/mm³ before 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.

DR. MELANIE THOMPSON: These single-tablet regimens both contain rilpivirine, a nonnucleoside reverse transcriptase inhibitor (NNRTI), and differ only in the use of TAF (Odefsey) or TDF (Complera). Neither is recommended as initial therapy in most people, largely because of potency and drug interactions associated with rilpivirine. Studies showed worse response when used as initial treatment in persons with viral loads of 100,000 copies/mL or more and CD4 counts of 200 cells/L or less, so they are not recommended in this population; 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 or exacerbation of pre-existing depression in some people. 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 and TDF, although there is little reason to initiate either of these drugs in 2024. Odefsey is the only NNRTI option containing TAF, while Complera is similar to Delstrigo (doravirine/TDF/3TC) but Delstrigo has fewer drug-drug interactions and no restrictions on viral load or CD4. See Descovy and Truvada for more information.

ACTIVIST JOEY WYNN: Although lighter on the side effects, this combo still has lots of drug-drug interactions based on people's feedback to me a few years back. Having to time it based on food intake makes this a less than stellar option for you in 2024. This is a hard pass in favor of several better options with little to no interactions or food requirements.

➤ **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, nausea, 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 and Truvada pages for more possible effects on kidney function. Increased monitoring for adverse events is recommended for people with ESRD who are taking Odefsey.

POTENTIAL DRUG INTERACTIONS

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 25 mg tablet in addition to Complera. Odefsey should not be taken with other medications that prolong QTc interval (these abnormal heart rhythms can make the heart stop) or medications with a known risk for torsades de pointes. Odefsey 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. Odefsey is one of the smallest STRs, which may be advantageous to individuals who have difficulty swallowing. 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.

MANUFACTURERS

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

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

ODEFSEY AWP

$4,144.75/month

COMPLERA AWP

$4,144.75/month

Symtuza

800 mg darunavir, 150 mg cobicistat, 200 mg emtricitabine, 10 mg tenofovir AF
DRV (PI), COBI (PK booster), FTC and TAF (two NRTIs)

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

✔ Recommended initial regimen in certain clinical situations; also for rapid ART for people who took Apretude (CAB-LA) for PrEP

➤ For people who took Apretude (CAB-LA) for PrEP, this regimen is recommended for rapid ART for someone newly diagnosed or entering care with no or minimal labs available.

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. Symtuza is HHS recommended for Rapid ART—to be started on the same day or within the same week of diagnosis before lab results are back.

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 severe 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 + 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 HBV 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, sildenafil (Viagra, Revatio, and generics), 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. The dose of colchicine will need to be adjusted. 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

A darunavir-based regimen is the only initiation treatment recommended by HHS for people who have used Apretude (CAB-LA for PrEP) when resistance data has yet to come back (rapid ART). That's because viral mutations conferring drug resistance to INSTIs like long-acting cabotegravir (found in Apretude and in Cabenuva) have been observed. CAB-LA stays in the body a very long time and drug levels may be too low to prevent infection and therefore may select for resistant virus. The other "clinical situations" mentioned in the HHS recommendation refers to people with adherence problems on their current HIV treatment. Symtuza is not the same as Prezcobix + 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." Darunavir-containing regimens had stronger evidence supporting their use than do regimens containing atazanavir (another PI on the market). Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

DR. MELANIE THOMPSON: Symtuza, a 4-drug protease inhibitor-based STR, is not recommended for initial therapy for most people with HIV due to the presence of the booster cobicistat, which causes many drug interactions. It is, however, now recommended for initial therapy for non-pregnant persons who acquired HIV following cabotegravir PrEP (Apretude) and who wish to start therapy before an INSTI genotype is available, or whose virus has resistance to INSTIs. This is based on the long "PK-tail" for cabotegravir which could select for INSTI-resistant viruses when the drug is present at levels too low to prevent infection. Symtuza is not recommended in pregnancy because 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 changing therapy. A recent study showed no benefit on weight in people changing from an INSTI-containing regimen to Symtuza.

For most people, the multitude of drug-drug interactions with COBI make unboosted INSTI regimens preferable. Possible side effects of Symtuza include diarrhea, nausea, abdominal discomfort, headache, rash and, less frequently, liver toxicity. Symtuza also is associated with elevated triglycerides and cholesterol (LDL and total.) A large observational study found an association between darunavir and cardiovascular disease. The average wholesale cost for Symtuza is the highest of all STRs and higher even than maintenance doses of Cabenuva.

ACTIVIST JOEY WYNN: Once a powerful option with a great profile against resistance, today this combination does not hold up against newer meds. This is mainly due to the booster, which increases almost every medication in the bloodstream; not a good look in 2024.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$5,611.48/month

Cabenuva

400 or 600 mg cabotegravir extended-release injectable suspension; 600 or 900 mg rilpivirine extended-release injectable suspension
CAB-LA (long-acting injectable INSTI)/RPV-LA (long-acting injectable NNRTI)

LA **Long-acting injectable regimen** containing an INSTI and an NNRTI

✔ HHS 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 with injections. ***See dosing schedules at*** positivelyaware.com/cabenuva.

For adults and adolescents age 12 and older weighing at least 77 pounds (35 kg) who are switching from a stable HIV regimen and 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 may be recommended before injections begin, consisting of a 30 mg tablet of cabotegravir (Vocabria) and a 25 mg tablet of rilpivirine (Edurant), which must be obtained from the contracted TheraCom Pharmacy. Oral rilpivirine must be taken with a meal. Initiate injections on the last day of oral lead-in or of your previous regimen. Smaller dose may cause less pain or discomfort. See package insert for instructions on using oral medications during planned or unplanned missed injections; oral medication should be taken until injections can be restarted. Prior ART regimens or oral cabotegravir and rilpivirine may be used for bridging missed injections, however, oral cabotegravir is only available from the contracted pharmacy, TheraCom, and all other ART will have to be obtained from another pharmacy. People may be given Cabenuva up to 7 days before or after the date scheduled for injections. Studies suggest injections for every 2-month dosing that are delayed for more than 1 week will lead to significantly lower drug levels and may lead to resistance. See package insert for instructions on missed doses (recommendations differ based on the dosing being used). Increased monitoring is recommended when CrCl is less than 30 mL/min. The effect of severe liver impairment on Cabenuva is unknown. Longer needles (not included in the dosing kit) are recommended for people with a BMI (body mass index) greater than 30. *Providers can see injection instructions at* positivelyaware.com/cabenuva.

➤ **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 can be used to assess for safety and tolerability, especially in individuals who have a history of rash, allergies or severe intolerances to past ART medications. The most common adverse reactions observed in 2% or more of people receiving Cabenuva in clinical trials were injection site reactions, fever, fatigue, headache, musculoskeletal pain, nausea, sleep disorders, dizziness, and rash. Serious post-injection reactions reported within minutes of administration (in less than 1% of people injected) may have been associated with inadvertent (partial) intravenous administration and began to resolve within a few minutes after injection in clinical studies: difficulty breathing, abdominal cramping, agitation, flushing, sweating, oral numbness, and changes in blood pressure. People should be observed for approximately 10 minutes after injections to monitor for potential reactions. Individuals with injection pain 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 has been reported with or without pre-existing liver disease or risk factors. People with underlying liver disease or marked elevations in transaminases may be at increased risk for rising transaminase level or worsening of current elevated levels. Monitor for signs of hypersensitivity. HHS guidelines recommend closely monitoring people with pre-existing psychiatric conditions on an INSTI. Data associate INSTIs with weight gain. There was a median weight gain of 3.3 pounds in Cabenuva trials. People with buttock implants or fillers may not be good candidates for this medication due to concerns about drug absorption.

POTENTIAL DRUG INTERACTIONS

Cabenuva cannot be taken with carbamazepine, eslicarbazepine, oxcarbazepine, phenobarbital, phenytoin, rifabutin, rifampin, rifapentine, systemic dexamethasone (more than one dose), or 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. Other medications that may increase the risk of QT prolongation when taken with Cabenuva, such as levofloxacin, moxifloxacin, aripiprazole, escitalopram, fluoxetine, donepezil and ondansetron, should be used with caution. Where possible, consider alternatives such as azithromycin, which increases rilpivirine concentrations less than other macrolides. Antacids should be taken at least 2 hours before or 4 hours after oral cabotegravir and oral rilpivirine, but do not interact with injections. 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, switch to 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 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 people should talk with their provider about opting for more frequent viral load testing or switching to a preferred or alternative 3-drug regimen recommended in pregnancy. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

DR. MELANIE THOMPSON: People with HBV will need to take additional oral HBV treatment and screening for HBV is essential before starting Cabenuva. Cabenuva can be given monthly or, at higher doses, every two months after two loading doses given one month apart. The FDA also has endorsed a "direct-to-inject" method, which decreases the risk of non-adherence to oral meds.

Balancing out the convenience of dosing every two months is the slightly higher incidence of drug resistance seen in clinical trials using the bimonthly regimen. It is important to consider whether you would be able to routinely get to clinic appointments every one or two months, which may be more often than your current schedule for HIV monitoring. Injections cannot be self-administered. *See Dr. Thompson's complete comments at* positivelyaware.com/cabenuva.

ACTIVIST JOEY WYNN: The great divide: Providers don't like it, in stark contrast to many people who want to move to injectables. Do you have an "on the go" lifestyle? Travel a lot for work? There are lots of other reasons to not want a bottle of HIV medication in your home. Pill fatigue? Is that bottle a reminder of your condition? Although definitely not for everyone, this is the next phase of evolution in HIV therapy. You can usually see extreme bias with many providers because this disrupts their existing clinic flow, and they give you 10 lame reasons why not to evaluate this option. Some studies suggest the vast majority of people who got on an injectable will never go back to taking pills. I've spoken at length with nearly 100 people in Florida who are on it, and none of them will go back to taking pills again. Understandably, there are issues of access for people on private insurance, clinic flow and limited distribution shortages meaning advocates need to demand improved pipeline delivery from the manufacturer so people can get what they need, want and require with fewer difficulties.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

28-day oral lead-in provided at no cost
Loading dose and every other month dosing (600 mg/900 mg): **$7,601.18**
Maintenance dose (400 mg/600 mg): **$5,067.46**/month

Sunlenca

927 mg subcutaneous injection lenacapavir
LEN (CAI)

CAI **Long-acting injectable** capsid assembly inhibitor

● For heavily treatment-experienced people whose current regimen is failing

STANDARD DOSE

Sunlenca is administered as two 463.5 mg (1.5 mL) subcutaneous injections (for a total dose of 927 mg) in the abdomen once every six months by a healthcare provider. It must be used as part of a regimen with another antiretroviral(s), the majority of which are taken daily orally.

There are two initiation dosing schedules, both consisting of a combination of lenacapavir tablets and subcutaneous injections. The first consists of the two subcutaneous injections + 600 mg oral LEN (two 300 mg tablets) on Day 1 and 600 mg oral LEN on Day 2. The second consists of 600 mg oral LEN on Day 1 and Day 2, 300 mg on Day 8 and the two injections on Day 15. The first maintenance dose begins six months later, give or take two weeks. If more than 28 weeks passes without the maintenance dose, re-start therapy with initiation dosing followed by the maintenance dose six months later.

Currently no dosage adjustment is recommended in patients with mild, moderate, or severe renal impairment; however, Sunlenca has not been studied in people with end stage renal disease with a CrCl less than 15mL/min. No dosage adjustment is recommended in people with mild or moderate hepatic (liver) impairment. Sunlenca has not been studied in people with severe hepatic impairment (Child-Pugh Class C).

DR. MELANIE THOMPSON: Lenacapavir appears to be a genetically fragile compound, requiring high adherence to background therapy and the use of background drugs with good activity against HIV. LEN also is subject to a fair number of drug-drug interactions that can persist for up to 9 months after the last dose.

The real promise of LEN, however, lies in pairing it with other injectable agents with similar half-lives to make a twice-yearly treatment regimen. Unfortunately, none of our currently approved drugs are ideal partners, but this is an area of active research, so stay tuned! Lenacapvir represents an important advance for HIV treatment, but a step backward in lowering the cost of ART.

See Dr. Thompson's complete comments at positivelyaware.com/drug-guides/sunlenca.

ACTIVIST JOEY WYNN: Lenacapavir is specifically aimed at heavily-treatment-experienced populations and long-term survivors. Since it was only FDA approved barely over a year ago, the jury is still out. This is another injectable in the long march towards a world of injectables and other long-acting agents. The future is definitely brighter with this new choice available. The jury is still out on this one; oddly, I've not heard from anyone on it yet, so I'm not sure how easily accessible it is.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Injection site reactions (generally considered mild and transient), nodules (bumps) and indurations (skin thickening). In the CAPELLA study, for Grade 3 and 4 laboratory abnormalities, 5% of participants experienced high blood sugar, 6% experienced excess sugar in urine and 13% experienced low creatinine clearance (eGFR) or high serum creatinine. These observed changes were related to the individual's diabetes or were either transient or unconfirmed. Nausea occurred in 4% of participants.

POTENTIAL DRUG INTERACTIONS

Do not take with carbamazepine, eslicarbazepine, oxcarbazepine, phenobarbital or phenytoin; rifampin, rifabutin, or rifapentine; pimozide; amiodarone, disopyramide, quinidine, bosentan, ivabradine, lomitapide, cisapride, flibanserin or St. John's wort. Start the following medications at the lowest dose, titrate carefully and monitor for safety: dexamethasone (do not take more than 16mg/day), hydrocortisone or cortisone; and lovastatin or simvastatin. Not recommended with ergot derivatives (dihydroergotamine, ergotamine and methylergonovine) or tadalafil (for pulmonary arterial hypertension, or PAH). See package insert for dose recommendations with erectile dysfunction drugs sildenafil and vardenafil. Dose adjustment may be needed for buprenorphine or methadone; initiate these medications by titrating to desired effect but use lowest feasible doses for initiation or maintenance and monitor effects. Coadministration with immunosuppressants such as cyclosporine, everolimus, sirolimus, or tacrolimus will require a dose adjustment for these medications and careful monitoring and dose titration based on drug levels – must be monitored very closely. Carefully monitor the effects of fentanyl and oxycodone; tramadol dose may need to be decreased. Avoid naloxegol (for opioid-induced constipation); if unavoidable, decrease its dose and monitor for adverse reactions. Use with caution with alfuzoson; if coadministration is necessary, monitor blood pressure closely and titrate dose of alfuzosin. Avoid use with beaquiline or quetiapine if possible; if benefits outweigh risks for coadministration, monitor liver function and ECG for QTc prolongation. Use caution with triazolam and oral midazolam (Versed). Use with caution if coadministering with warfarin; monitor INR and titrate warfarin dose as clinically indicated. If giving with the psych medications buspirone, paroxetine, brexpiprazole, iloperidone, lumateperone, lurasidone or trazodone, monitor for side effects and may need to use lower dose of psych medication. Would avoid use with clopidogrel but if coadministration is required, monitor for clopidogrel adverse effects. Would try to avoid coadministration with lidocaine, propafenone, dronedarone, diltiazem, verapamil, and digoxin but if necessary, would monitor closely for adverse effects. Use with caution if coadministering with eplerenone or ranolazine; a dose adjustment of these meds will be necessary if taking at same time as Sunlenca. Use caution if coadministering with colchicine used for gout – will require a dose adjustment and monitoring of colchicine. Okay to take with the antacid famotidine (Pepcid), the cholesterol drug rosuvastatin (Crestor), tenofovir alafenamide (TAF, found in Descovy and other medications), tenofovir DF (TDF, found in Truvada and other medications), HCV medications and the antifungal voriconazole. Other acid-reducing medications can also be used, such as H2 blockers (including Axid, Tagamet and Zantac) and proton pump inhibitors (including Nexium, Prevacid and Prilosec). Certain HIV medications cannot be given with Sunlenca because a drug interaction will render it ineffective: do not coadminister with efavirenz, etravirine, nevirapine, or boosted or unboosted atazanavir; these medications are rarely prescribed today. 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

Sunlenca long-acting subcutaneous injection—administered just once every six months—is the first in its drug class. It must be used with other HIV medications as the background therapy. 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. Sunlenca is a capsid assembly 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. 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. At this time, there aren't sufficient data to support the initiation of Sunlenca during pregnancy. People who become pregnant while on Sunlenca do not necessarily have to switch to another regimen, but may undergo closer monitoring of viral load. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

Two 1.5 ml injections (SQ):
$23,400.00/month

Rukobia

600 mg fostemsavir
FTR (AI)

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

▼ For people who are heavily treatment-experienced

STANDARD DOSE

One tablet twice daily, with or without 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

The most common side effect is nausea in 10% of study participants. Other side effects, observed less often, were diarrhea, fatigue, and headache. Use with caution in people who have a history of QTc prolongation (these abnormal heart rhythms can make the heart stop). 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. Clinically relevant increases in serum creatinine have occurred in patients taking Rukobia who have risk factors for reduced renal (kidney) function (including pre-existing history of renal disease and/or taking other medications at the same time that are known to cause increases in creatinine. A causal relationship between Rukobia and increased serum creatinine has not been established. Increases in direct bilirubin have also been observed. Cases of clinical significance were uncommon and were typically transient, occurred without increases in liver enzymes, and resolved on continued Rukobia therapy.

POTENTIAL DRUG INTERACTIONS

Dose modification of fostemsavir is not required when co-administering with atazanavir/ritonavir (Reyataz + Norvir), cobicistat (Tybost), darunavir/cobicistat (Prezcobix), darunavir/ritonavir (Prezista + Norvir) with and without etravirine (Intelence), maraviroc (Selzentry), raltegravir (Isentress HD), ritonavir, ibalizumab (Trogarzo), lenacapavir (Sunlenca) or tenofovir DF (found in Truvada). 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 or rifapentine, antimycobacterial drugs 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, phenobarbital 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 elevated liver enzyme levels. 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 designed to be used in highly treatment-experienced people, who typically have fewer options for HIV treatment than those just starting 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. 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. Watch a video of its mechanism of action at youtu.be/WnreXE-TVi8. 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.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$10,205.72/month

DR. MELANIE THOMPSON: Fostemsavir, an oral attachment inhibitor that prevents HIV from entering the T cell, is approved only for people who are treatment-experienced. The drug must be taken twice daily, but is generally well tolerated, with mild nausea as the most common side effect. Fostemsavir should not be taken with the androgen receptor inhibitor enzalutamide, some seizure and tuberculosis medicines, mitotane or St. John's wort. It 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 should not be used in pregnancy due to insufficient data.

Fostemsavir is the most expensive oral HIV drug with a wholesale acquisition cost of $8,027 per month, likely due to the relatively small market for the drug. There is a patient assistance program for people with commercial insurance that is intended to make the drug affordable to people despite high cost. If you are on this drug, be sure you check coverage before you change insurance, as some plans are not covering fostemsavir.

ACTIVIST JOEY WYNN: Rukobia (fostemsavir) is the first drug in a new class called attachment inhibitors. This is a vital choice for those heavily treatment-experienced individuals who are running out of options. This is for use only in highly treatment-experienced people, so definitely not a choice if this is your first time choosing the right regimen.

Selzentry

maraviroc
MVC (EI)

EI **Entry inhibitor:** CCR5 antagonist

▼ For heavily treatment-experienced people who have CCR5-TROPIC virus

■ Generic and brand name available for 50 mg and 300 mg tablets. Only brand name available for oral solution 20 mg/mL.

STANDARD DOSE

The recommended dose varies depending on other medications being taken but will be either 150, 300, or 600 mg twice daily (available in 150 mg and 300 mg tablets). Can be taken with or without food. Must be taken in combination with another antiretroviral(s).

Approved for adults and children weighing at least 4.4 pounds (2 kg) and having a creatinine clearance of at least 30 mL/min (measure of kidney function). Available in a 20 mg/mL oral solution. Selzentry for children is dosed based on body weight. See the package insert or HHS guidelines for weight-based dosing. The oral solution should be administered using the included press-in bottle adapter and oral dosing syringe.

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).

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). Not recommended with eslicarbazepine, oxcarbazepine, rifapentine or 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 HHS 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 coreceptor on the outside of a CD4 cell, and shuts down this point of entry for the virus. Most people have acquired R5 virus initially, and then over time, X4 and mixed viruses may predominate. The tropism test needed is now generally paid for by public health departments, Medicare, and private insurances. ViiV may cover the payment for the Trofile test under certain circumstances.

Selzentry seems to have minimal impact on lipid levels. HHS 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

AVERAGE WHOLESALE PRICE

150 mg, 60 tablets:
$2,076.10/month
300 mg, 60 tablets:
$2,076.10/month
generic: price not available at press time

DR. MELANIE THOMPSON:
The only approved CCR5 entry inhibitor, maraviroc is not for initial therapy and is very rarely used. It may be helpful, however, for people whose virus has substantial resistance and who struggle to put together a viable regimen. Selzentry only works against HIV that uses the CCR5 receptor, requiring a viral tropism test before using the drug. The drug requires twice-daily dosing, making adherence more challenging, and it has many drug-drug interactions requiring dose adjustments of Selzentry or the other drug. Selzentry 25 mg and 75 mg tablets have been discontinued.

ACTIVIST JOEY WYNN:
Selzentry, or maraviroc, is only for use in highly treatment-experienced people, with many past failed regimens. Selzentry is one pill, twice daily, with or without food. Given other available options, I don't believe anyone would want to choose Selzentry, even someone who might be highly treatment-experienced and who might have limited treatment options unless this is their last "new" option to add with other drugs.

Trogarzo

ibalizumab-uiyk (IBA)

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

▼ For people who are heavily treatment-experienced

STANDARD DOSE

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

The first dose takes 90 seconds if pushed or at least 30 minutes if infused. If no infusion-related adverse events occur, subsequent doses can be given as an IV push over 30 seconds or as an IV infusion over 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 receiving their first dose. If no administration-associated adverse reaction is noted, the post-administration observation time can be reduced to 15 minutes for subsequent doses.

For the IV push: The undiluted solution should be administered immediately. Trogarzo should be administered in the cephalic vein of the patient's arm. For the IV infusion: Once diluted, the Trogarzo solution should be administered immediately. If not administered immediately, store at room temperature for up to 4 hours or refrigerated for up to 24 hours. If refrigerated, allow diluted solution to stand at room temperature for at least 30 minutes, but no more than 4 hours, prior to administration.

Trogarzo must be given with an optimized background regimen (OBR). An OBR consists of the best antiretroviral therapy that can be selected for a person 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 maintenance dosing (800 mg) can be resumed 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 in 2021 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

The FDA approval is for heavily treatment-experienced (HTE) individuals with resistance to multiple HIV drug classes, in combination with an optimized background regimen (OBR), for people who are failing their current regimen. 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. 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 a doctor's office or an infusion center. People must be on time. It is expensive because of the cost of the drug 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. The undiluted IV push dosing requires less time and supplies to administer.

Other long-acting HIV drugs are on the way and may be studied in combination with Trogarzo as well. Sunlenca (SEE that drug page) has been approved for heavily treatment-experienced people and can be combined with Trogarzo. 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 by the company to be 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.

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.

Thera Patient Support can assist with private or government insurance coverage, including AIDS Drug Assistance Programs (ADAPs), 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.

DR. MELANIE THOMPSON: Ibalizumab is a "post-attachment" inhibitor that stops HIV from entering the CD4 cell. It is only used for people with multidrug resistant HIV who cannot otherwise construct a viable regimen. It requires intravenous (IV) infusions or IV push every 2 weeks. There is preliminary evidence (presented in a poster at CROI 2024) that intramuscular (in the muscle) dosing may also work, although Trogarzo is not FDA approved in this manner. It is the most expensive antiretroviral drug ever approved, with administration costs not included. The pricing is accompanied by a patient assistance program that intends to shield individuals—but not the healthcare system—from much of the financial burden. Trogarzo has no known drug-drug interactions.

ACTIVIST JOEY WYNN: Ibalizumab is the first drug in a new class called CD4-directed post-attachment inhibitors. It blocks the virus from entering CD4 cells; for use only in highly treatment-experienced people, meaning they have no other realistic options. More convenient oral or injectable HIV drugs are in development for highly treatment-experienced people, but until those drugs are approved. Trogarzo remains a vital lifeline for them to buy time until the next new option.

MANUFACTURER

TaiMed USA

DISTRIBUTED BY

Theratechnologies Inc.
theratech.com; trogarzo.com

AVERAGE WHOLESALE PRICE

$3,435.60 per box (2 vials); 10 vials for loading dose and four vials for continuing dose (every two weeks)

Tivicay

50 mg dolutegravir
DTG (INSTI)

INSTI **Integrase strand transfer inhibitor**

★ Recommended as a component of initial regimen for most people with no history of Apretude (CAB-LA) for PrEP

➤ Recommended as a component of rapid ART for someone newly diagnosed or entering care with no or minimal labs available.

STANDARD DOSE

One 50 mg tablet once daily, with or without 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, with or without 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) from a different 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 with or without 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 between 30.8 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 in 2021, the pediatric ODYSSEY/PENTA-29 trial did not observe the weight gain observed 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. HHS 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, including vitamins, or buffered medications. It can be taken with iron- or calcium-containing supplements/vitamins 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, eslicarbazepine, 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. Dose Tivicay twice daily if using with rifampin, carbamazepine, efavirenz, Aptivus/Norvir, or Lexiva/Norvir. 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.

DR. MELANIE THOMPSON: Dolutegravir is recommended as initial therapy for any adult with HIV (in combination with TAF or TDF and FTC or 3TC), and as a preferred drug in pregnancy, based on the IMPAACT 2010 trial. Updated data have found no statistically significant difference in the rate of neural tube defects when dolutegravir is taken during conception compared with regimens not containing dolutegravir. Folate supplementation decreases the risk of neural tube birth defects and is routinely recommended for all pregnant persons.

There is ongoing debate about whether weight gain is associated with dolutegravir, as has been seen in some studies. Weight should be monitored and healthy eating and physical activity should be part of a wellness routine when beginning HIV treatment. The substantial benefits of INSTIs in potency and rapidity of viral load suppression, low pill burden, high genetic barrier to resistance, improved tolerability and decreased drug interactions are felt to outweigh the potential risk of weight gain, which generally can be managed. 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. Dolutegravir increases blood creatinine levels by about 0.1-0.15 mg/dL due to changes in tubular secretion of creatinine in the kidneys without any actual kidney damage.

Dolutegravir levels can be decreased by taking sucralfate or supplements and antacids containing aluminum, calcium, magnesium, zinc or iron, so you should 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 JOEY WYNN: Tivicay is safe, effective, and tolerable. It is potent, relatively easy to take and with "little to no" side effects from anyone I know taking this. In south Florida, the "Dolly Dezzy" combo (dolutegravir/Descovy) is a great choice if you're okay with taking pills. On the down side, for some people, weight gain is a thing, for real. Have a serious conversation with your medical provider to see if this is the right choice for you.

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 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 HIV protease inhibitor (PI) drugs. It is also a very small tablet, making it easier to swallow. Tivicay along with Truvada or Descovy is a preferred drug regimen for PEP (post-exposure prophylaxis—preventing HIV acquisition after a potential exposure), as well as two other regimens: Biktarvy or Isentress HD plus Truvada or Descovy.

Recommended as part of a preferred initial regimen in pregnancy (Tivicay plus Descovy or Epzicom or Truvada; Triumeq is also a preferred initial regimen). 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: **$2,557.03**/month

Isentress HD (and Isentress)

raltegravir
RAL (INSTI)

INSTI Integrase strand transfer inhibitors

✔ Each is HHS recommended as a component of initial regimen in certain clinical situations with no history of Apretude (CAB-LA) for PrEP

STANDARD DOSE

ISENTRESS HD: Two 600 mg film-coated tablets once daily, with or without food, for individuals new to HIV therapy (treatment-naïve) or who are virologically suppressed (have undetectable viral load) on an initial regimen containing raltegravir.

ISENTRESS: One 400 mg film-coated tablet twice daily, with or without food, for people with HIV treatment experience or individuals who are new to HIV therapy.

Must be taken in combination with another antiretroviral(s) from a different 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 4.4 pounds (2 kg). Both Isentress HD and Isentress can be taken with or without food.

Isentress (but not Isentress HD) pediatric formulations are available as an oral suspension. Isentress dosing is based on weight for children less than 55 pounds; see package insert for dosing and mixing instructions. Dosing of the granules for oral suspension is not equivalent to tablets. Do not substitute 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, headache and fatigue. The side effect profile in children is comparable to adults. INSTIs have been associated with weight gain.

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 (such as depression, sleep disturbances and dizziness) in some retrospective cohort studies and case series. The HHS 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 considered by some as a relative inconvenience. According to HHS HIV treatment guidelines, raltegravir was 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 along with Truvada or Descovy is a preferred drug regimen for PEP (post-exposure prophylaxis—preventing HIV acquisition after a potential exposure), as well as two other regimens: Biktarvy or Tivicay plus Truvada or Descovy. Isentress, but not Isentress HD, 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, but the powder formulation remains a preferred initial regimen for newborn and infant treatment and PEP following birth.

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

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

Isentress HD and Isentress not available on formulary used

DR. MELANIE THOMPSON: Raltegravir, the oldest INSTI, is no longer recommended for initial therapy by HHS or IAS-USA guidelines panels because newer INSTIs are less susceptible to viral resistance and can be given once daily with lower pill burden in most situations. The HD formulation allows two pills to be taken once daily, but it is not available as an STR. In pregnancy, raltegravir must be given at 400 mg twice daily. When given with rifampin for tuberculosis, the dose of raltegravir is 800 mg twice daily.

ACTIVIST JOEY WYNN: About 17 years ago Isentress came onto the scene as the first integrase strand transfer inhibitor (INSTI). It is currently prescribed for initial therapy in certain situations, but not for the majority of folks just starting treatment. Pregnancy is the biggest reason for using this older but easy to take treatment; it's still a viable option, so don't count this well tolerated option out just yet. In retrospect, I've not heard anyone taking Isentress HD complain about weight gain like other agents in its class. I hope someone does some kind of formal study to confirm if this is a true (beneficial) characteristic of this particular agent.

Prezista

darunavir
DRV

PI Protease inhibitor

- Generic and brand name available for 600 mg and 800 mg oral tablets.
  Brand available only for 75 mg and 150 mg oral tablets and 100 mg/mL oral suspension.

Prezcobix

800 mg darunavir,
150 mg cobicistat
DRV (PI), COBI (PK booster)

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

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

➤ For people who took Apretude (CAB-LA) for PrEP, **recommended as a component for rapid ART** for someone newly diagnosed or entering care with no or minimal labs available

STANDARD DOSE

PREZISTA: Two different doses available. One 800 mg tablet + 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 + 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 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) from a different drug class. Do not use either drug in people with severe liver impairment. Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Darunavir should be used with caution by people with known severe sulfonamide allergy. 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. Report symptoms of illness to a health care provider. Protease inhibitors can cause increased risk for bleeding in hemophiliacs. Measure liver function before starting darunavir and then monitor. No dose adjustment necessary for darunavir with mild to moderate liver disease.

POTENTIAL DRUG INTERACTIONS

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. 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. Take lower dose of colchicine. 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. 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. Monitoring is recommended for co-administration with drospirenone or colchicine. 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. Start metformin at lowest dose and titrate based on tolerability and clinical effect. Apixaban dose may need to be adjusted.

DR. MELANIE THOMPSON: Darunavir 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. A large observational study found darunavir to be associated with higher cardiovascular risk than atazanavir. Ritonavir should be used as a booster in pregnancy, and Prezcobix should not be used.

ACTIVIST JOEY WYNN: Once a strong first-line option, darunavir is now relegated to a few minor situations for a very select few. Boosters are no longer acceptable as a first line defense in my opinion, so this is a trusted option for heavily treatment-experienced people in need of something powerful; I know a few dozen women in Florida still taking this strong option. If I had to go back on a protease-containing regimen again, Prezcobix would be the only one I would even consider, as my personal experience with it was better than any of the other protease-containing regimens.

MORE INFORMATION

Darunavir is found in the single-tablet regimen Symtuza (see that page). A darunavir regimen is the preferred, and only, recommended initial treatment in people with acute or recent HIV infection who have a history of using Apretude for PrEP. 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:
$2,514.35/month
800 mg, 30 tablets:
$2,514.35/month

PREZCOBIX AWP

$2,873.84/month

Reyataz

atazanavir sulfate
ATV

PI Protease inhibitor

■ Generic and brand name available for 200 mg and 300 mg oral tablets. Brand name only available for 50 mg oral packet. Generic only available for atazanavir 150 mg oral tablets.

Evotaz

300 mg atazanavir, 150 cobicistat
ATV (PI), COBI (PK booster)

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

✔ Recommended as a component of an 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 + 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 doses. Take Norvir or Tybost at the same time as Reyataz. Swallow capsules whole—do not open or mix with anything. Pediatric dose of 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). 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) from a different 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.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Side effects include nausea, ocular icterus (yellowing of the eyes), and jaundice. 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.

ATAZANAVIR: Kidney laboratory testing should be performed on all individuals before starting Reyataz, and continued during treatment. Rarely, chronic kidney disease has been observed. People with underlying liver disease should have hepatic testing done before starting an atazanavir regimen and be monitored. 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.

DR. MELANIE THOMPSON: Atazanavir-based regimens are no longer recommended in most circumstances 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. Acid blockers can't be used with atazanavir, and the drug must be taken with food. On the bright side, large cohort studies have not found an association with cardiovascular disease. In pregnancy, atazanavir 400 mg must be used with ritonavir as a booster.

ACTIVIST JOEY WYNN: Not sure why this is even being discussed anymore. Not a worthy option for anyone at this point in time.

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 (PPIs, like Aciphex, Dexilant, Nexium, Protonix, and Prevacid) and H2-receptor antagonists (H2RAs, like Pepcid, Zantac, and Tagamet) can stop Reyataz from being absorbed. Treatment-experienced people should not take PPIs while on atazanavir. See package insert for antacid dosing adjustment. Take chewable antacids with food two hours before or one hour after atazanavir dose. Not recommended to coadminister with lenacapavir (boosted or unboosted) due to significant increases in lenacapavir levels (up to 4-fold). 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.

MORE INFORMATION

Yellowing of the eyes is a common reason for discontinuation. A ritonavir-boosted atazanavir regimen is an alternative once-daily PI-based treatment in pregnancy, but requires increased dosing in the second or third trimester. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider.

MANUFACTURER

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

REYATAZ AWP

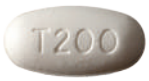
200 mg, 60 capsules:
$1,755.91/month
300 mg, 30 capsules:
$1,739.30/month

GENERIC ATAZANAVIR AWP

150 mg, 60 capsules:
$1,502.76/month
300 mg, 30 capsules:
$1,502.76/month

EVOTAZ AWP

$1,926.56/month



Intelence

200 mg etravirine
ETR (NNRTI)

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

✔ For treatment-experienced people with viral strains resistant to an NNRTI

■ Generic and brand name available for 600 mg. Generic available only for 50 mg and 200mg oral tablets.

STANDARD DOSE

One tablet, twice daily with a meal. Taking Intelence without food could result in a 50% decrease in drug absorption and may lead to HIV drug resistance. Must be taken in combination with another antiretroviral(s) from a different drug class.

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.

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 ages 2–18, 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 6–18, 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 Norvir. Intelence should be avoided with Tivicay unless administered with one of the following combinations: Reyataz/Norvir, Prezista/Norvir, or Kaletra. Fostemsavir levels may be decreased by 50%, so it is recommended to be used with caution. If using fostemsavir with ritonavir-boosted darunavir, use with caution and monitor for side effects due to the potential for increased levels of fostemsavir. Coadministration with lenacapavir has not been studied, but is not recommended as it may impair lenacapavir efficacy. 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 carbamazepine, phenobarbital, phenytoin, rifapentine, rifampin, or the herb St. John's wort. Use with caution when combined with the antifungals Diflucan (fluconazole) and Vfend (voriconazole). 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 atorvastatin, fluvastatin, lovastatin, pitavastatin, and simvastatin. Monitor the effectiveness of Coumadin (warfarin) and adjust dose as needed based on clinical response. Alternatives to clopidogrel 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 have prescribed Intelence once daily (two of the 200 mg tablets) based on clinical trials that showed 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 adherence. Although the HHS 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. The pharmacokinetics (PK) of etravirine are not significantly altered during pregnancy, and no dosage adjustment is necessary. The PK data demonstrated 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 never approved for initial therapy and is rarely used, largely having been superseded by rilpivirine and doravirine, both of which can be taken once daily with lower pill burden and many fewer drug interactions. Etravirine cannot be taken with lenacapavir, atazanavir/cobicistat, or dolutegravir (unless darunavir + ritonavir is also taken). It can increase levels of many drugs for heart rhythm abnormalities and the anticoagulant warfarin. It should not be taken with many drugs for tuberculosis, seizures, hepatitis C or St. John's wort. Among the statins, only pitavastatin and rosuvastatin should be taken with etravirine. Given the many other excellent options available, there are few reasons to use etravirine today.

ACTIVIST JOEY WYNN: Intelence is approved for use only for highly-treatment-experienced people. Compared to today's selection of ARV regimens, there is no longer a niche for this option in my opinion.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

100 mg, 120 tablets:
$1,762.22/month
etravirine generic:
100 mg, 120 tablets:
$1,609.11/month
Intelence: 200 mg, 60 tablets:
$1,762.22/month
etravirine generic:
200 mg, 60 tablets:
$1,609.11/month

Edurant

25 mg rilpivirine
RPV (NNRTI)

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

✔ HHS 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 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 100,000. Must be taken in combination with another antiretroviral(s) from a different 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.

A long-acting injectable form is available; SEE Cabenuva page.

According to HHS 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 people who don't meet these levels. 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).

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. This regimen is approved to replace oral ART in patients with virologic suppression and no history of resistance to RPV or INSTIs. 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

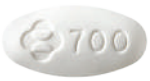
Janssen Therapeutics
edurant.com
(800) JANSSEN (526-7736)

AVERAGE WHOLESALE PRICE

$1,620.26/month

DR. MELANIE THOMPSON: Oral rilpivirine is primarily used as a component of the STRs Odefsey, Complera and Juluca. It should only be initiated when viral load is below 100,000 copies/mL and CD4 is at least 200 cells/mL and should be taken with a meal of at least 390 calories. Rilpivirine can be associated with depression or headache, liver toxicity (especially in people with hepatitis B or C), rash (including a severe hypersensitivity reaction) and increased risk of kidney stones or gallstones. There are many important drug-drug interactions with oral rilpivirine. It requires acid for absorption and should not be taken with antacids, acid blockers or proton-pump inhibitors such as Prilosec, Pepcid or Nexium. It can lower the levels of other drugs, such as methadone, and rilpivirine levels are decreased by some seizure and tuberculosis medicines, dexamethasone and St. John's wort. There are other drug interactions, so it's a good idea to discuss any drugs you take, including over-the-counter meds and supplements, with your HIV care provider. A long-acting injectable formulation of rilpivirine is paired with injectable cabotegravir as Cabenuva. Drug interactions for the injectable formulation differ from those of the oral drug.

ACTIVIST JOEY WYNN: Edurant is a once-daily pill that must be taken with food. Edurant has lots of drug-drug interactions. Given other available options, Edurant is not an obvious choice for most people; there are just too many easier to take regimens available now. #HardPass.



Pifeltro

100 mg doravirine
DOR (NNRTI)

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

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

STANDARD DOSE

One tablet, once daily with or without 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) from a different drug class.

Approved for adults and children who weigh at least 77 pounds (35 kg). Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. 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 (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. 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 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 known to be 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. According to HHS guidelines: "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. However, it is predicted that blood levels of Pifeltro are lower in pregnant women, which may reduce the effectiveness of the medication. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

DR. MELANIE THOMPSON: Doravirine was not tested head-to-head against INSTIs prior to approval, therefore is not recommended for first-line therapy in most circumstances by HHS and IAS-USA guidelines. It is combined with TDF and 3TC as Delstrigo. In clinical trials, doravirine was associated with less nausea and rash and fewer neuropsychiatric side effects such as dizziness, abnormal dreams, and sleepiness, than efavirenz, and with less diarrhea than ritonavir-boosted darunavir. LDL, triglycerides and total cholesterol increased with efavirenz and ritonavir-boosted darunavir but decreased with doravirine. In a cross-study analysis, at week 48, 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), 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. Doravirine is not recommended in pregnancy due to insufficient data.

The monthly wholesale acquisition cost of doravirine is $1,597.

ACTIVIST JOEY WYNN: Pifeltro can be used regardless of viral load, taken without food, and does not interact with proton pump inhibitors. It is definitely an option for people who developed drug resistance to other NNRTIs. Pifeltro allows people to take it with other newer combinations. In resource-constrained jurisdictions, this option may save the bank if funding is limited.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$2,012.40/month

Sustiva

600 mg efavirenz
EFV (NNRTI)

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

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

■ Generic and brand name available for 600 mg. Generic available only for 50 mg and 200 mg oral tablets.

STANDARD DOSE

One tablet once daily on an empty stomach, preferably at bedtime (food can increase the incidence of central nervous system, or CNS, side effects). Must be taken in combination with another antiretroviral(s) from a different 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 or talk to your doctor. 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 pregnant individuals 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. It is not recommended to be taken with Sunlenca, since it's expected to lower Sunlenca levels by more than 50%. Increase Kaletra to two 200/50 mg tablets + 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. People who are treatment-experienced should not take Reyataz with Sustiva, but for those who are treatment-naïve, 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, atorvastatin, pravastatin, and simvastatin 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 (these abnormal heart rhythms can make the heart stop) 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 used by most providers and are not recommended by HHS or IAS-USA guidelines due to multiple side effects, many of them affecting the central nervous system, including suicidality (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. Efavirenz may be given during pregnancy, but data from IMPAACT 2010 show more frequent growth stunting with efavirenz than with dolutegravir, and dolutegravir is now preferred.

ACTIVIST JOEY WYNN: Causes serious side effects such as nightmares, depression, and suicidal ideation, making it difficult to tolerate. It must be taken on an empty stomach. Given other available options, Sustiva is not an obvious first choice for most people.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

Sustiva 600 mg, 30 tablets: **$1,117.90**/month
generic: 600 mg, 30 tablets: **$1,073.18**/month
Sustiva 200 mg, 90 capsules: **$1,176.74**/month
generic: 200 mg, 90 capsules: **$1,043.37**/month
Sustiva 50 mg, 30 capsules: **$98.12**/month
generic: 50 mg, 30 capsules: **$88.31**/month

Descovy

200 mg emtricitabine, 25 mg tenofovir AF
FTC and TAF (two NRTIs)

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

★ HHS recommended as a component of initial regimen for most people

➤ **Recommended as a component for rapid ART** for someone newly diagnosed or entering care with no or minimal labs available.

STANDARD DOSE

One tablet once daily, with or without food. All doses, adult and pediatric, must be taken in combination with another antiretroviral(s) from a different drug class.

For adults and children weighing at least 31 pounds (14 kg). For children who are not also taking a boosted protease inhibitor, use one tablet for children weighing at least 25 kg to less than 35 kg (55 to 77 pounds) and use one pediatric tablet (120 FTC/15 mg TAF) for children weighing at least 14 kg to less than 25 kg (31 to 55 pounds).

Take a missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. 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. Tell your provider about any pain in extremities, persistent or worsening bone pain, as well as any concerning changes in urinary habits. 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. Bone mineral density (BMD) tests may be recommended in people with history of or risk factors for bone fractures or osteoporosis. 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, 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 components of 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. Descovy (as well as Truvada or Epzicom) are recommended with Tivicay as a preferred complete regimen in pregnancy. 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

$2,590.94/month

DR. MELANIE THOMPSON:

Descovy contains tenofovir alafenamide (TAF), the newer version of tenofovir. Along with Truvada, it is recommended for initial therapy for most people when combined with an INSTI anchor drug. TAF/FTC is also included in Symtuza, Genvoya 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. Descovy is marketed as being "safer" than Truvada, but the kidney and bone changes with TDF are often not clinically significant for young, healthy people without comorbidities, and for those who are not taking ritonavir or cobicistat. LDL and HDL cholesterol changes and weight gain are higher with Descovy than Truvada, primarily because TDF is associated with decreased LDL and HDL as well as weight loss. Like Truvada, Descovy is active against hepatitis B, owing to the activity of both TAF and FTC. Because of data from IMPAACT 2010, TAF/FTC is now recommended with dolutegravir as preferred drugs in pregnancy by the HHS perinatal and adult guidelines and the IAS-USA guidelines.

ACTIVIST JOEY WYNN:

Although smaller and easier to swallow than its predecessor, Truvada, both backbone therapies have some side effect profiles for a small percentage of people taking it. Those side effects are often overstated and exaggerated, but it's a real concern for folks with chronic kidney disease and kidney problems to begin with.

Epzicom

600 mg abacavir, 300 mg lamivudine
ABC and 3TC (two NRTIs)

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

Ziagen

300 mg abacavir
ABC (NRTI)

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

★ Each is HHS 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

One Epzicom tablet once daily, with or without food. Two Ziagen tablets once daily (or one 300 mg tablet twice daily), with or without food. Both must be taken in combination with another antiretroviral(s) from a different drug class.

Epzicom is approved for adults and children weighing 55 pounds (25 kg) or more. Ziagen is 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.

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 30 mL/min) due to lamivudine component, or those with moderate or severe liver impairment due to abacavir component. Alternative doses may be obtained by using the individual components of this medication as needed. Ziagen 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 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 warning card that comes with Epizom and Ziagen. 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. 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 and kept with you. 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. HSR might be confused with flu, but symptoms of HSR usually worsen, very slowly, and with every dose.

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). 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.

DR. MELANIE THOMPSON: Brand name Epzicom and Ziagen tablets have been discontinued by ViiV due to the availability of generic abacavir and abacavir/3TC. Abacavir and 3TC also are coformulated with dolutegravir as Truimeq (see Triumeq.) Abacavir was once an important medication for HIV treatment, but it always has been problematic because of the risk of life-threatening abacavir hypersensitivity. Results of the genetic marker HLA-B*5701 are required before dosing with abacavir to decrease this risk. Anyone with prior abacavir hypersensitivity should never take even one dose of abacavir again and should ensure that their medical chart is marked as "allergic to abacavir" (although this reaction is not a true allergy). Observational studies have found conflicting evidence on whether abacavir is associated with cardiovascular disease. The FDA says the evidence is "inconclusive," however, guidelines panels acknowledge a potential risk. In early clinical trials, the most common side effects with abacavir were nausea, headache, malaise and fatigue, vomiting and dream/sleep disorders. At present, abacavir is mainly used for people who can't take tenofovir-containing regimens, especially because of kidney disease. Dovato or nuke-sparing regimens like Juluca or Cabenuva are also options for some people.

ACTIVIST JOEY WYNN: Epzicom and Ziagen have not aged well. With the shadow of cardiovascular issues still lurking in the lexicon of advocates, the allergic hypersensitivity and the required lab tests needed, abacavir is simply too complicated to compete with so many easier to tolerate, simplified regimens around today. Definitely ill advised to take if you have hepatitis B. Epzicom is recommended by DHHS as one of the preferred NRTI combination components of HIV treatment in pregnancy. As for Ziagen, I personally do not believe this is a viable option in today's choices. But maybe for a select few in certain circumstances. 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 better for you.

POTENTIAL DRUG INTERACTIONS

Alcohol can increase levels of abacavir, and therefore can increase the possibility of side effects. 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 Epzicom, is a DHHS recommended initial therapy for most people. Otherwise, the guidelines recommend Descovy or Truvada over Epzicom as the backbone NRTI component of an HIV drug combination for first-time therapy. Recommended as part of a preferred initial regimen in pregnancy (Tivicay plus Descovy or Epzicom or Truvada; Triumeq is also a preferred initial regimen). Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

MANUFACTURERS

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

AVERAGE WHOLESALE PRICE

Epzicom:
$1,550.05/month
generic:
$1,395.05/month
Ziagen 300 mg, 60 tablets:
$670.37/month
generic: abacavir 300 mg, 60 tablets:
$602.71/month

Emtriva

200 mg emtricitabine
FTC (NRTI)

■ Generic and brand available for 200 mg oral tablets. Brand name only available for 10 mg/mL oral solution.

Epivir

150 or 300 mg lamivudine
3TC (NRTI)

■ Generic is available.

NRTI **Nucleoside reverse transcriptase inhibitors** (nucleosides, or "nukes")

★ Each is HHS recommended as a component of initial regimen for most people

STANDARD DOSE

One Emtriva capsule once daily, with or without food, for adults and children regardless of age. One 300 mg Epivir tablet once daily (or one 150 mg tablet twice daily), with or without food. Emtriva and Epivir for children is dosed based on body weight; see the package insert. Epivir can be used by children at least 3 months of age. Emtriva is also available as an oral solution (10 mg/mL) (cotton candy flavored) for children and adults who cannot swallow the capsules. The dosing for the oral solution is as follows: 3 mg/kg for children 0–3 months, 6 mg/kg for children aged 3 months to 17 years, and 10 mg/kg for adults 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. See package inserts for guidance on dosing in the setting of kidney impairment. Emtriva and Epivir must be taken in combination with another antiretroviral(s) from a different 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.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

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 FTC or 3TC, because they 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. Rare skin discoloration (darkening of the skin on the palms and the soles) can occur with Emtriva and was more frequent in children, but is generally mild and not medically concerning.

POTENTIAL DRUG INTERACTIONS

May be used with hepatitis C drugs such as Epclusa, Harvoni or Zepatier, depending on the other components in the HIV regimen. Avoid using 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

These drugs are used almost exclusively as a component of combination tablets. They are similar to each other, and both treat HIV and HBV and have the same drug resistance profile. This means 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). 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). Recommended as part of a preferred initial regimen in pregnancy (Tivicay plus Descovy or Epzicom or Truvada; Triumeq is also a preferred initial regimen). 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. Sometimes, drug resistance that the virus develops against FTC or 3TC 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 FTC or 3TC treatment in combination with other antiretrovirals after resistance develops. 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. The Emtriva 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.

DR. MELANIE THOMPSON: Emtriva (emtricitabine; FTC), is similar to Epivir (lamivudine; 3TC), including in their resistance profiles. Their signature mutation, M184V, causes loss of antiviral activity but also increases the antiviral activity of tenofovir or AZT. They are considered interchangeable by guidelines panels for treatment, but not for prevention because 3TC has not been studied as part of a PrEP regimen. FTC is generally coformulated with TDF or TAF as a dual nuke regimen, or as part of many STRs, while 3TC is coformulated with abacavir or generic TDF; with dolutegravir as the STR Dovato; and with doravirine and TDF as the STR Delstrigo. An unusual side effect, hyperpigmentation of palms and soles, was noted with FTC in some early clinical trials, yet rarely occurs "in real life." Both drugs require dosage adjustment according to kidney function. Both have some activity against hepatitis B but should not be used alone for hepatitis B treatment.

ACTIVIST JOEY WYNN: Emtriva is one of the most convenient HIV drugs available; very small so it is easy to take, with few to no side effects so it is not hard to keep up without problems, and beneficial mutations (which make the virus less able to reproduce as quickly as the wild type virus). Consider it a first cousin to Epivir. Epivir is still one of my favorite medications, due to lack of side effects, tiny size and, like Emtriva, makes the virus less "fit" to replicate. Epivir has been around since about 1995; one of the first HIV medications available, it is the only one still in use from the OG.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE (EMTRIVA)

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

MANUFACTURER

ViiV Healthcare
viivhealthcare.com
(877) 844-8872

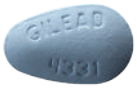
AVERAGE WHOLESALE PRICE (EPIVIR)

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

Truvada

200 mg emtricitabine, 300 mg tenofovir DF
FTC and TDF (two NRTIs)

■ Generic is available.



Cimduo

300 mg lamivudine, 300 mg tenofovir DF
3TC and TDF (two NRTIs)

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

★ Both recommended as component of initial regimen for most people when combined with Tivicay; recommended as component of initial regimen in certain clinical situations when used in other combinations

Viread

300 mg tenofovir DF
TDF (NRTI)

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

★ Recommended as a component of initial regimen for most people

■ Generic and brand name available for 300 mg oral tablets.
Brand name available only for oral powder 40 mg/GM and 150 mg, 200 mg, and 250 mg oral tablets.

➤ All three recommended as a component of rapid ART for someone newly diagnosed or entering care with no or minimal labs available.

STANDARD DOSE

Truvada, Cimduo: One tablet once daily, with or without food, for adults and children weighing at least 77 pounds (35 kg). Viread: One tablet once daily, for adults and children at least 2 years old weighing at least 22 pounds (10 kg). All must be taken in combination with another antiretroviral(s) from a different drug class.

In children weighing 37–76 pounds (17–34 kg), Truvada dose is based on body weight (see package insert for weight-based dosing). Pediatric Truvada tablets are available in the following FTC/TDF dosages: 100/150 mg, 133/200 mg and 167/250 mg. In children, Viread dose is based on body weight (see package insert). Viread tablets are available in the following dosages: 150 mg, 200 mg, 250 mg and 300 mg tablets, and oral powder (40 mg/g in 60 g packets). Truvada and Viread tablets can be dissolved in water, grape juice, or orange juice with minor stirring and pressure from a spoon.

Take a missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. Dosing frequency needs to be adjusted for people who have decreased kidney function. The dose of Truvada and Viread 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 or if you are on dialysis. Truvada is not recommended in HIV-negative individuals if CrCl is below 60 mL/min (see Truvada for PrEP page). Cimduo should not be used if CrCl is less than 50 mL/min or if you are on dialysis.

DR. MELANIE THOMPSON: TDF has a high genetic barrier to resistance and potent activity against hepatitis B. Cimduo includes generic TDF and 3TC. They are essentially the same drugs made by different generic manufacturers but they are considered "brand" drugs because they are combinations for which there is no other brand precedent. The good news for consumers is that this allows copay cards to be used to lower out-of-pocket costs. The bad news is that this allows companies to maintain drug prices that are less than that of Truvada, but still unnecessarily high. 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 the boosters ritonavir or cobicistat. TDF also lowers LDL and HDL cholesterol and is associated with a bit of weight loss. Generic TDF/FTC came at a very high price, but is now available as low as $25–35 per month.

ACTIVIST JOEY WYNN: Truvada does not have a negative impact on cholesterol levels and weight. Cimduo is a hybrid between generic and brand medicines, and definitely have a niche in the private insurance payor world. The optimal groups who would benefit are people during pregnancy and people seeking an NRTI therapy. Neither group has been approved for PrEP at this time, but it would be worth the effort to make it happen.

➤ **SEE THE INDIVIDUAL DRUGS CONTAINED IN CIMDUO AND TRUVADA:** Epivir, Viread and Emtriva.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Overall well tolerated, but some people may experience headache or gastrointestinal distress. Rash and depression may occur with Cimduo. Rare skin discoloration on palms and soles may occur with Truvada. TDF is associated with long-term decreases in bone mineral density (BMD). TDF can cause kidney toxicities. Tell your provider about any pain in extremities, persistent or worsening bone pain, as well as any concerning changes in urinary habits. Routine monitoring of estimated creatinine clearance, serum phosphorus, urine glucose, and urine protein should be performed in 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 these medications. Monitor liver enzymes closely in people co-infected with HBV and, if appropriate, initiation of anti-hepatitis B therapy may be warranted upon drug discontinuation. Call your health care provider right away if you develop any signs of hepatitis. Truvada contains lactose, which can cause some abdominal discomfort.

POTENTIAL DRUG INTERACTIONS

Reyataz/Norvir and Prezista/Norvir increase TDF concentrations, so monitoring is recommended for TDF-associated adverse events, particularly decreases in kidney function. Avoid taking TDF with drugs that negatively affect the kidneys, including chronic use or high doses of anti-inflammatory drugs for pain such as aspirin, Advil or Motrin (ibuprofen) and Aleve (naproxen). TDF may be used with hepatitis C drugs Harvoni or Zepatier, depending on the third drug in the HIV regimen; monitor for TDF toxicities if used with Epclusa. TDF should not be given with adefovir or unboosted atazanavir. For Cimduo, avoid using sorbitol-containing medicines because of 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

Recommended as part of a preferred initial regimen in pregnancy (Tivicay plus Descovy or Epzicom or Truvada; Triumeq is also a preferred initial regimen). Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

MANUFACTURERS

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

AVERAGE WHOLESALE PRICE

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

Viread: $1,504.20/month
generic: $1,215.94/month

MANUFACTURERS

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

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

AVERAGE WHOLESALE PRICE

Cimduo: $1,354.28/month

Norvir ritonavir RTV

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

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

■ Generic and brand name available for 150mg oral tablets. Brand name only available as Norvir 100mg oral packet.

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; 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 the tablet does not. Liquid formulation available (80 mg/mL) in peppermint caramel flavor, but it is not very palatable. The liquid's taste 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 discomfort, 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. Do not take with alfuzosin, amiodarone, cisapride, clopidogrel, dronedarone, eplerenone, flibanserin, flecainide, ivabradine, lomitapide, lumateperone, lurasidone, propafenone, oral midazolam, triazolam, pimozide, propafenone, quinidine, ranolazine, Revatio, rifapentine, rifampin, silodosin, suvorexant, ticagrelor, vorapaxar, voriconazole, ergot derivatives, ziprasidone, or the herb St. John's wort. Carefully weigh benefits of coadministering tamsulosin and monitor for possible side effects or adjust dose if indicated. 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, eslicarbazepine, oxcarbazepine, phenobarbital, and phenytoin. Use calcium channel blockers (amlodipine, nifedipine, and others) with caution. If coadministering with pimavanserin, buprenorphine, or everolimus, a dose reduction may be required as well as additional monitoring. 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. Do not use with avanafil. 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. Do not coadminister with atazanavir and lenacapavir. 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 a protease inhibitor that has activity against HIV but now is used only as a booster to raise the levels of certain protease inhibitors. Because of this boosting effect, there are many, many drug interactions with ritonavir, some of them dangerous. It's important to check with your HIV provider, if possible, before taking other drugs, including over-the-counter medications and supplements. Always inform anyone who is prescribing non-HIV 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, but don't try to manage them yourself.

Diarrhea, nausea and vomiting are the most common side effects of ritonavir. Liver toxicity also has been seen, and ritonavir raises triglyceride levels. Ritonavir also commonly causes the odd side effects of tingling of the mouth and taste disturbance.

Ritonavir is used to boost levels of nirmatrelvir in the anti-COVID drug Paxlovid. 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. There is an interaction with maraviroc, so check with your HIV prescriber before taking Paxlovid with maraviroc. If you have side effects while taking Paxlovid, be sure to contact your HIV care provider. 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. In addition to the HIV drug interactions checker mentioned above, the University of Liverpool also has a COVID-19 drug interactions checker, covid19-druginteractions.org. The FDA drug interaction guide for Paxlovid is at fda.gov/media/158165/download. IDSA recommendations are here: idsociety.org/globalassets/covid-19-real-time-learning-network/patient-populations/hiv/oral-covid-tx-considerations-for-people-with-hiv-and-hcv.pdf.

ACTIVIST JOEY WYNN: Protease boosting with low-dose Norvir was a thing. Even at low doses it caused GI problems, especially diarrhea; definitely not a drug to ever use again.

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.

MANUFACTURER

AbbVie
norvir.com; (800) 633-9110

AVERAGE WHOLESALE PRICE

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

Tybost

150 mg cobicistat
COBI (PK booster)

PKE **Pharmacokinetic enhancer (booster)**

✔ Used only as a booster for other drugs; recommended as a component of an 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 is not interchangeable with Norvir. Tybost interacts with many drugs. Do not take with alfuzosin, amiodarone, avanafil, cisapride, clopidogrel, dapagliflozin/saxagliptin, dihydroergotamine, dofetilide, dronedarone, eplerenone, ergotamine or ergot derivatives, flibanserin, irinotecan, ivabradine, simvastatin, lomitapide, lovastatin, lumateperone, lurasidone, methylergonovine, midazolam, ranolazine, rifabutin, rifampin, rifapentine, rivaroxaban, pimozide, ticagrelor, triazolam, oral midazolam, Revatio, silodosin, suvorexant, triazolam, vorapaxar, or St. John's wort. Carefully weigh benefits of coadministering tamsulosin and monitor for possible side effects or adjust dose if indicated. 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. Itraconazole (antifungal) and clarithromycin (antibiotic) may increase Tybost concentrations. Tybost may also increase Biaxin levels. Tybost should not be given with clarithromycin in patients with CrCl less than 50mL/min. Rifabutin and some anti-seizure medications, such as carbamazepine (Tegretol), eslicarbazepine, oxcarbazepine, phenobarbital, and phenytoin (Dilantin) may decrease Tybost drug levels and should not be coadministered. If coadministering with colchicine, a lower dose may be required as well as extra monitoring. Do not coadminister with colchicine in patients with hepatic or renal impairment. 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 drug interactions similar to 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 care 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, a pharmacokinetic (PK) booster with no activity against HIV, is generally coformulated with the protease inhibitors atazanavir and darunavir or the integrase inhibitor elvitegravir. Like the other PK booster, ritonavir, there are a boatload of drug interactions, some dangerous. COBI, however, is not interchangeable with ritonavir in all circumstances. COBI has most of the drug interactions of ritonavir and some that are different. For example, COBI should not be used twice daily with darunavir 600 mg, but is paired with darunavir 800 mg once daily. You should be sure your HIV care provider knows all of the drugs you are taking, including over-the-counter medications and supplements, and be sure that anyone who prescribes drugs for you knows that you are on cobicistat. You can look up drug interactions at hiv-druginteractions.org but managing them is tricky, so be sure to discuss with an HIV care provider.

Cobicistat-containing regimens should not be taken during pregnancy due to inadequate drug levels of COBI and boosted drugs in the second and third trimester. If you are on a cobicistat-containing regimen and are pregnant or contemplating pregnancy, discuss with your HIV care provider.

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

The COVID-19 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 JOEY WYNN: Tybost is a booster, with the same side effect problems as Norvir, the other booster. Simply ask, "What other options are available for me?" and keep moving.

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 HHS 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

$339.96/month

POSITIVELY AWARE

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Apretude

cabotegravir 600 mg extended-release injectable suspension; CAB-LA (INSTI)

PrEP **Long-acting PrEP (pre-exposure prophylaxis)** for the prevention of HIV

★ FDA approved only 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. Individuals may be given Apretude up to 7 days before or after the date the individual is scheduled to receive injections every 2 months.

Daily oral lead-in therapy for about a month to determine tolerability is optional before injections begin, consisting of a 30 mg tablet of Vocabria. Initiate injections on the last day of oral lead-in. Individuals who were on daily oral PrEP with Descovy or Truvada can transition directly to Apretude injections once their HIV-negative status is confirmed. 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 have 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. A longer two inch needle (not included in the dosing kit), may be required for people with a higher BMI (body mass index) of 30 or more. Do not administer Apretude injections at any site other than gluteal muscle because the effects of drug absorption at other sites is unknown. At this time, injections should only be administered by a healthcare professional.

- 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

Optional oral lead-in can be used to assess for safety and tolerability, especially in individuals who have a history of rash, allergies or severe intolerances to past medications. 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 cannot be taken with rifampicin, rifapentine, carbamazepine, eslicarbazepine, oxcarbazepine, phenytoin, phenobarbital or St. John's wort. 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 is not known. Methadone dose may need to be adjusted. Antacids should be taken at least 2 hours before or 4 hours after oral cabotegravir. 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

Apretude is the first long-lasting injectable PrEP medication—dosed just once a month for 2 months and then every other month thereafter. Individuals should be tested for HIV infection before receiving every injection. Updated guidelines recommend HIV-negative test results should be confirmed with a negative HIV viral load test as well. 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." 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." Advice on preparing for injection site reactions is included along with the risk of developing drug resistance and the importance of keeping up follow-up appointments if stopping PrEP for any reason. For individuals who want to discontinue Apretude but who also have ongoing risk of sexual and injection HIV exposure, guidelines recommend these individuals be provided another highly effective HIV prevention method following their last injection. HHS guidelines have a section on the use of cabotegravir-LA for people with a history of injection drug use. Apretude does not prevent or treat hepatitis B. Apretude is not recommended for people who are pregnant. Because cabotegravir-LA has been detected in systemic circulation for up to 4 years 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: In clinical trials, Apretude was superior to oral Truvada in preventing new HIV infections among gay and bisexual men and transgender women, and among cisgender women. Injection site reactions were very common but rarely caused anyone to stop taking the drug. It is important to test for HIV before each dose of CAB because missing an acute HIV infection while on CAB as PrEP could result in cross-resistance to all integrase inhibitors and limit treatment options. Currently, CDC recommends an HIV RNA viral load test before every dose, but this may change, so consult guidelines frequently. CAB levels decline after 2 months to the point that it can't prevent HIV but may be associated with drug resistance for people who acquire HIV after taking the drug. Modeling studies suggest that low levels of CAB may persist for up to three or four years (especially in ciswomen), thus heightening concerns about viral resistance. As a result, an INSTI genotype is recommended for anyone who acquires HIV after exposure to CAB PrEP. If it is important to begin HIV treatment before the genotype result is available (such as in the setting of acute infection), HHS and IAS-USA guidelines recommend beginning with a boosted darunavir regimen (Prezcobix + TDF or TAF and FTC or 3TC, or Symtuza). This could be changed to an INSTI-based regimen if no resistance is found, in order to avoid drug interactions with cobicistat. Long-acting CAB for PrEP could be a major advance in our ability to end the HIV epidemic, if only it can be broadly accessible to the most heavily impacted groups, especially Black and Hispanic/Latino populations. A great deal of public and provider education is needed, and the high cost of the drug as well as the operational logistics of administration are significant obstacles.

ACTIVIST JOEY WYNN: This revolutionary formulation will have a huge impact in dramatically reducing new cases of HIV domestically. Barriers removed can include the burden of taking pills and going to the pharmacy every month for pick up, co-pay costs, and all the other headaches of getting and taking pills, as well as the stigma some people experience seeing HIV medicine bottles in the home. Now hopefully, we'll get to see a majority of folks staying on their PrEP year round. The biggest barriers are insurance plan coverage and distribution access, particularly in the north east. Let's get some advocacy going to iron out these distribution problems so people can get what they need in all the injectables as a class.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com
(877) 844-8872

AVERAGE WHOLESALE PRICE

$4,440 per vial, based on WAC

Descovy for PrEP

200 mg emtricitabine, 25 mg tenofovir alafenamide
FTC and TAF (two NRTIs)

PrEP Pre-exposure prophylaxis (PrEP) - oral medication

★ 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, with or without food.

Take a missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. 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. Bone mineral density (BMD) tests may be recommended in people with history of or risk factors for bone fractures or osteoporosis. 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, adefovir, 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 is 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. Individuals should be tested for HIV at least every 3 months while taking Descovy for PrEP. 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 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 and there was a significant legal challenge at the time of publication. 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/prevention/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 at (877) 505-6986, or GO TO gileadadvancingaccess.com. PrEP Facts: Rethinking HIV Prevention and Sex is a closed Facebook group for people interested in or currently on PrEP, and their allies.

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

DR. MELANIE THOMPSON: The DISCOVER trial in cisgender gay and bisexual men and transgender women found Descovy to be noninferior to Truvada as PrEP. It was a bad decision not to study these regimens in ciswomen, people who inject drugs, and transgender men, and consequently, Descovy is not approved for these groups, thus widening disparities. Gilead's PURPOSE-1 trial of Descovy vs. lenacapavir for PrEP is beginning in Africa for young cisgender women and girls, and will fill in some of the evidence gap for Descovy as well as evaluating LEN for PrEP. Luckily, Truvada remains the first choice for PrEP for many people, and the price is decreasing over time owing to generic competition. Descovy was associated with lower rates of biomarkers of kidney toxicity and bone density loss, but slightly more weight gain, and higher LDL and HDL cholesterol than Truvada, which lowers LDL and HDL and may cause mild weight loss. 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 a hepatitis flair if Descovy is stopped without other drugs on board to treat hepatitis B. For insured individuals, there should be no out-of-pocket cost for the drug or PrEP services (office visits and lab monitoring including STI screening) due to an "A" rating from the United States Preventative Services Task Force (USPSTF). Uninsured people still struggle for PrEP access, although the federal End the HIV Epidemic initiative has opened some doors to free drugs through its Ready. Set. PrEP. program. Much more is needed, including full funding for the national PrEP program initially proposed by President Biden in March 2022, and making a commitment that all programs will be equity-based.

ACTIVIST JOEY WYNN: 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 this is their only true option based on concerns about kidney function and bone issues. There should be no out-of-pocket cost for this drug or for PrEP services. Resources abound as to getting and removing barriers to co-pays and other financial impediments.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$2,590.94/month

Truvada for PrEP

200 mg emtricitabine, 300 mg tenofovir DF
FTC and TDF (two NRTIs)

PrEP Pre-exposure prophylaxis (PrEP) - oral medication

★ FDA approved for the prevention of HIV (PrEP)

■ Generic is available.

STANDARD DOSE

For HIV-negative adults and adolescents weighing at least 77 pounds (35 kg), one tablet once daily, with or without food. See more information for non-daily dosing.

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. (Note: this is different from Truvada for HIV treatment.)

➤ 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. Truvada should not be given with adefovir. 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. Individuals should be tested for HIV infection at least every 3 months while taking Truvada for PrEP. CDC PrEP guidelines list non-daily dosing that can be used. This includes PrEP on demand: two pills 2–24 hours before sex followed by one pill 24 hours later and another pill 48 hours later (also called 2-1-1 or intermittent PrEP; GO TO cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf, see pages 55–57). 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 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 and there was a significant legal challenge at the time of publication. 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. GO TO nastad.org/prep-access for an FAQ. 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 at (877) 505-6986, or GO TO gileadadvancingaccess.com. HHS 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/prevention/prep.html. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

DR. MELANIE THOMPSON: Generic TDF/FTC is now available at low cost in the U.S. It should be noted that generic TDF/3TC is not approved for use as PrEP. The adherence challenges of taking a pill a day have always been the Achilles heel of oral PrEP. Headache, abdominal pain and decreased weight were the most common side effects attributable to Truvada in PrEP trials, and a few more people stopped the 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. In spite of this, Truvada remains a safe and effective PrEP option for most people, especially younger people without preexisting kidney disease or low bone density. It should be noted that tenofovir levels are increased with the hepatitis C drug Harvoni (ledipasvir/sofosbuvir) and close monitoring of TDF-related toxicities is recommended. People with hepatitis B may experience a hepatitis flare if Truvada or TDF/FTC is stopped without other drugs on board to treat hepatitis B. For insured 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 (USPSTF). We badly botched the rollout of PrEP in the U.S.; far too many people who could benefit still lack access to PrEP, with wide disparities by race, ethnicity and gender.

ACTIVIST JOEY WYNN: Truvada—although controversy abounds, this work horse has helped many a person maintain their viral load back in the day, and now it can help reduce the chances of acquiring HIV. Still a viable option, TDF has some side effects, but so do the other options. Have several conversations with a variety of medical professionals before deciding which prevention option is right for you. TDF may be better than TAF when it comes to cholesterol and weight gain; this remains the first choice for PrEP for many people, including people who are contemplating pregnancy. Remember, even if your only option is generic Truvada, it will work well, too.

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 the 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.

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, a reconstituted Egrifta SV dose should be discarded.

Body fat redistribution to the abdomen, called central adiposity, can develop as a result of HIV, antiretroviral therapy, and/or growth hormone (GH) deficiency. Central adiposity in HIV has a higher amount of visceral abdominal fat. This visceral abdominal fat is inside the abdomen surrounding internal organs like the stomach, liver, intestines, etc. Excess visceral abdominal fat may be linked with serious health issues like cardiovascular disease, non-alcoholic steatohepatitis (fatty liver disease), diabetes, or increased mortality. People with this condition describe symptoms of a regular bloating feeling, difficulty bending down/reduced flexibility, or anxiety/depression due to reduced physical activity and dissatisfaction with body image.

Central adiposity may be a complicated term to accurately describe, but it is different from obesity. To understand if you have excess visceral abdominal fat, talk with your HIV health care provider. Simple measurements of waist circumference and hip circumference can determine if you are likely to have excess visceral abdominal fat.

Different from all other growth hormone (GH) treatments, Egrifta SV is similar to the natural form of human growth hormone-releasing hormone (GHRH), that stimulates the pituitary gland to produce and secrete more of the body's own GH, mostly during sleep. Egrifta SV reduces visceral abdominal fat while preserving subcutaneous fat, which is important for some individuals. A response typically appears within three months and continues to improve in time with a sustained effect at 12 months.

The effect on excess visceral abdominal fat was seen in two Phase 3 clinical trials. A post-hoc responder analysis has shown, on average, 31% of decrease in visceral abdominal fat in those who respond. The reduction in visceral fat alone resulted in an average 1.85-inch smaller waist circumference. It is important to note that visceral abdominal fat can return a few months after tesamorelin is discontinued as the underlying causes are still present.

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 Egrifta SV; 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 and should be discontinued in critically ill people.

The most common side effects include pain in legs, arms, and muscles. Long-term cardiovascular safety has not been studied. Refer to the Egrifta SV prescribing information for additional information.

CAP & PAP INFORMATION

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 egriftasv.com.

MANUFACTURER

Theratechnologies, Inc.
egriftasv.com

Thera Patient Support:
(833) 23-THERA; (833-238-4372)
egriftasv.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 people living with HIV 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 effective, 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 people 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.

ISTOCK

Applying for PAPs
In 2012, the Department of Health and Human Services (HHS), along with seven pharmaceutical companies, the National Alliance of State and Territorial AIDS Directors (NASTAD), and community stakeholders, developed a common patient assistance program application form that can be used by both providers and patients. This combines common information collected on each individual company's form to allow individuals to fill out just one. Once the form is completed, case managers or individuals then submit the single form to each individual company, reducing the overall amount of paperwork necessary to apply for a patient assistance program.

In addition to serving as a special PAP for ADAP waiting list clients, HarborPath 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.	
Biktarvy, Complera, Descovy, Emtriva, Genvoya, Odefsey, Stribild, Sunlenca, Truvada and **Tybost**	**Gilead Sciences** 800-226-2056; 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. **Sunlenca:** $9,600.	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 on January 1
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.	Enrollment is valid until coupon expires, 12/31/2024
Trogarzo	**Theratechnologies** 833-238-4372; trogarzo.com	$7,500 per year Contact program for details Determined on a case-by-case basis	
Apretude, Cabenuva, Dovato, Juluca, Retrovir, Rukobia, Selzentry, Tivicay, Tivicay PD, Triumeq, Viracept and **Ziagen**	**ViiV Healthcare** 844-588-3288; ViiVConnect.com	**Apretude,** $7,850; **Cabenuva,** $13,000; **Dovato** and **Juluca,** $6,250; **Tivicay,** $5,000; **Triumeq** and **Rukobia,** $7,500 per year/per patient maximum. **Lexiva, Retrovir, Selzentry, Viracept,** and **Ziagen:** $4,800 per year/per patient maximum.	Automatic renewal on January 1
Viread	**Patient Access Network Foundation** 866-316-7263; panfoundation.org	Maximum benefit is $3,250 per year. Patients may apply for a second grant during their eligibility period subject to availability of funding. All HIV funds are closed but may be reopened if new funding becomes available. Can only get on a wait list.	Reapply each year

PATIENT ASSISTANCE PROGRAMS (PAP)

DRUGS COVERED	MANUFACTURER AND CONTACT INFORMATION	FINANCIAL ELIGIBILITY
Kaletra	**AbbVie** 800-222-6885 kaletra.com; abbviepaf.org	$90,360 (600% 2024 FPL)
Aptivus, Viramune XR	**Boehringer Ingelheim** 800-556-8317; boehringer-ingelheim.us	$75,300 (500% 2024 FPL)
Biktarvy, Complera, Descovy, Emtriva, Genvoya, Odefsey, Stribild, Truvada and **Tybost**	**Gilead Sciences*** 800-226-2056 gileadadvancingaccess.com	$75,300 (500% 2024 FPL)
Edurant, Intelence, Prezcobix, Prezista and **Symtuza**	**Janssen Therapeutics** 800-652-6227; jjpaf.org	$45,180 (300% 2024 FPL)
Delstrigo, Isentress, Isentress HD, and **Pifeltro**	**Merck and Co.** 800-727-5400 merckhelps.com; isentress.com	$60,240 (400% 2024 FPL)
Trogarzo	**Theratechnologies** 833-238-4372; trogarzo.com	Based on individual insurance Call program for details
Apretude, Cabenuva, Combivir, Dovato, Epivir, Epzicom, Lexiva, Juluca, Retrovir, Rukobia, Selzentry, Tivicay, Triumeq, Viracept and **Ziagen**	**ViiV Healthcare** 844-588-3288; ViiVConnect.com	$75,300 (500% 2024 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.

Are clinicians listening?

BY **BRIDGETTE PICOU**

Healthcare as a whole comes with pitfalls that are both inherent to the systems that run it and that are a result of the people in those systems. Medical practitioners are human, which means they are subject to the same attitudes and prejudices that have existed since the practice of medicine began. Threaded throughout its history is misogyny and sexism.

Medical misogyny refers to sexism and/or gender bias in medicine, medical practices and medical diagnoses. As far back as Hippocrates and his use of the word "hysteria" (derived from the Greek word meaning uterus) to describe any set of unusual behaviors related to women and health, there is a foundation of distrust and disregard in how women's care needs are perceived. Combined with the persistence of stereotypes, this first form of gender bias in medicine lends itself to the pervasiveness of a theme in healthcare. Providers aren't listening to women.

Frequently, women's pain is dismissed and glossed over as being in our head. Rather than accepting pain symptoms or complaints for what women say it is, they are passed off as emotion or hysteria. The McKinsey Health Institute estimates that while women may live longer than men, they will spend an average of nine years in poor health. This is called the "health span" rather than the "life span." In HIV, women are underrepresented in clinical trials and dismissed as being hard to reach or hard to work with. Women are often diagnosed later than men with HIV because of attitudes about what is appropriate for women to do with their bodies sexually, and perceptions about who is vulnerable to, and who acquires, HIV. Such attitudes delay testing and receiving information about prevention methods like PrEP. Studies also show that women tend to have a lower adherence to antiretroviral therapy than men.

ISTOCK

I could quote study after study, but the real question is *why*? We are light years away from Hippocrates and 375 B.C, and early experimentation on women. Our understanding of the human body is exponentially broader and things that once would have been considered a miracle are now everyday procedures. Gender-specific roles, and the power dynamics of those roles could be a factor. In addition to why, we should also be asking *what we do about it*. It comes down to a combination of *listening* and *asking* the *right questions*.

Open communication is foundational to the relationship between a clinician and a patient. Often, people get caught up in *listening to respond* as opposed to *listening to hear and understand*. While it is true that providers see hundreds of patients in a month and may have "seen it all," the underlying nuances of any health condition can only be found through thoughtful questions and active listening. While the volume of patients and the limited time allotted to see them can make that seem impossible, it's truly not. Practicing a pattern of listening in the same way providers practice medicine makes it possible.

This is part of shared decision making and has been shown to improve health outcomes and satisfaction with care. Showing active listening skills and creating dialogue is how trust is built. The mistrust of clinicians in women to know how their bodies feel leads to delays in treatment, misdiagnosis, and may cloud whether informed consent is actually informed. This leads women to distrust healthcare and those providing the care. Mistrust is lack of faith based on a belief, while distrust is lack of faith based on experience or knowledge. There is a subtle difference between the two, but they build upon and reinforce each other. Responding appropriately to individual concerns and the provision of clear, easily understandable information can influence women to follow a care plan and adhere to medication regimens. Utilizing the five dimensions or Five "A's" of access framework—approachability, acceptability, availability, accommodation and appropriateness of response—are great ways to build a system of listening to and hearing women. Treating women as individuals is also critical. Small steps that take us away from medical misogyny and toward equitable and quality healthcare for women.

BRIDGETTE PICOU, LVN, ACLPN, is a licensed vocational and certified AIDS Care Nurse in Palm Springs, California. She works for The Well Project-HIV and Women as their stakeholder liaison. Bridgette is a director at large for ANAC (the Association of Nurses in AIDS Care), and a sitting member of the board of directors for HIV & Aging Research Project-Palm Springs (HARP-PS). Bridgette's goal is to remind people that there are lives being lived behind a three- or four-letter acronym.

What's new in the HIV treatment pipeline

BY **LARRY BUHL**

With an HIV vaccine still elusive (but still possible), research continues for longer-acting, effective regimens that are less susceptible to resistance and easier to take. Here are a few ongoing treatment trials to watch in 2024.

PHASE 1b

Long-acting injectable regimen
Gilead Sciences

Twice-yearly injections of lenacapavir and bNAbs considered safe

At the 2024 Conference on Retroviruses and Opportunistic Infections (CROI), key findings were presented from a study evaluating the safety and efficacy of Gilead's lenacapavir (LEN) with broadly neutralizing antibodies (bNAbs) in a twice-yearly injection.

A phase 1b study published in *The Lancet HIV* demonstrated that a combo of LEN + two broadly neutralizing antibodies (bNAbs), teropavimab (GS-5423, TAB) and zinlirvimab (GS-2872, ZAB), both under development by Gilead, maintained virologic suppression for six months with twice-yearly dosing. Following up on these results, an additional cohort was added to evaluate the regimen in an expanded population of virologically suppressed PWH who were on ARV therapy for at least 18 months and who had high sensitivity to either TAB or ZAB. **The goal was to determine whether either bNAb would impact the safety profile or efficacy of the combined therapy.**

Eleven participants (ages 28–63 years) were randomized and treated, and at 26 weeks 8 out of 10 remaining participants maintained viral suppression (HIV viral load ≤50 copies/mL). Of two participants who had virologic rebound, one had sensitivity to TAB and was diagnosed with acute COVID-19 at the time of rebound, and the other had sensitivity to ZAB; both had HIV RNA below 100 copies at week 26.

"The long-acting combination of LEN+TAB+ZAB was well tolerated, with a favorable safety profile," the authors wrote. "All participants in the higher ZAB dose group maintained viral suppression for 6 months, which suggests that more inclusive sensitivity criteria may be appropriate for treatment studies of LEN+TAB+ZAB when higher bNAb levels are maintained."

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Study of the lenacapavir + TAB + ZAB combination now advances to a phase 2 trial (NCT05729568), which will continue evaluating the combination's safety and efficacy in virologically suppressed participants.

PHASE 2

Long-acting injectable
ViiV Healthcare

CAB-LA + bNAbs safe for ART maintenance

In a growing wave of research into combining bNAbs with traditional antiretroviral therapy, a **phase 2 study pairing a bNAb infusion every two months with a monthly cabotegravir injection shows that the combination is safe**, researchers presenting the data at CROI said. The trial, studying the combination of VRC07-523LS, a bNAb targeting the HIV CD4-binding site, and long-acting cabotegravir (CAB-LA) for maintenance ART, showed that most participants maintained viral suppression; however, 14% prematurely discontinued the regimen, including 5 virologic failures and 1 death (unrelated to the study).

PHASE 2

Weekly oral regimen
Gilead Sciences

Islatravir + lenacapavir: effective, but adverse events common

Researchers at CROI presented 24-week data evaluating a once-weekly oral combination of islatravir (ISL) and lenacapavir (LEN), both made by Gilead, another investigative compound that could help decrease pill burden and increase adherence. (SEE "Two pills a week or two shots a month" in the MAY+JUNE 2024 PA.)

In the study, 104 virologically suppressed adults with a median age of 40 years on bictegravir/emtricitabine/tenofovir alafenamide fumarate (B/F/TAF, brand name Biktarvy) were randomized to one of two groups: weekly oral ISL 2 mg + LEN 300 mg, or continuing the daily B/F/TAF regimen. The study found that at week 24, ISL+LEN maintained viral suppression and was well tolerated. "The ISL 2 mg dose showed no clinically significant decreases in CD4+ T cell counts as were seen previously with higher daily, weekly, and monthly doses of ISL," researchers wrote. Comparing the two groups of participants, 49 (94.2%) on ISL+LEN and 48 (92.3%) taking B/F/TAF maintained viral suppression at week 24. However, two (3.8%) and four (7.7%) participants, respectively, had no data due to discontinuation or missing visits, and adverse events occurred in 39 participants (75.0%, the most common, 13.5%, being diarrhea) taking ISL+LEN and 38 (73.1%) on the B/F/TAF regimen. No serious (Grade 3 or 4) adverse events related to study drug were reported.

PHASE 2

Daily oral regimen
ST Pharm Co. Ltd.

ALLINIs may be longer-lasting therapy

Allosteric integrase inhibitors (ALLINIs) target the noncatalytic sites of the viral integrase and interfere with integrase-viral RNA interaction during viral maturation, an approach that, if effective, could be longer lasting than current therapies that could improve the quality of life for people living with HIV. The study, now in phase 2a (NCT05869643), is assessing the antiviral effect, safety, tolerability, and pharmacokinetics of one ALLINI, pirmitegravir, which was developed by ST Pharm Co. Ltd., in treatment-naïve adults. Phase I data showed a once-daily dose of pirmitegravir to be well tolerated. Phase 2 data are expected this year.

PHASE 2/3

Daily oral regimen
Gilead Sciences

Bictegravir and lenacapavir once-daily combo

Nearly 10 percent of people with HIV (PWH) on treatment take two or more pills per day. The ARTISTRY-1 trial (NCT05502341) has been studying the effect of combining bictegravir (BIC) and lenacapavir (LEN) in a once-daily tablet, which could reduce the pill burden for them. Although single-tablet regimens for HIV have been available for more than a decade, some people cannot take those regimens.

In the study, 128 virally-suppressed PWH on multi-tablet regimens were randomly selected to either receive once-daily tablets of bictegravir 75 mg + lenacapavir 25 mg or remain on their current treatment. In the 24-week data presented at CROI, **people who switched to daily oral BIC+LEN still had undetectable levels of HIV in their blood and had few, and mild, side effects**.

"These data support the continued evaluation of a combination of BIC and LEN to optimize treatment in [virally suppressed] PWH who are receiving complex regimens," the authors wrote. This single-tablet regimen will be further evaluated in the Phase 3 portion of the ARTISTRY-1 study.

Bictegravir and lenacapavir are manufactured by Gilead Sciences.

PHASE 3

Daily oral regimen
Gilead Sciences

Biktarvy for PWH with comorbidities

A study evaluating the efficacy and safety of Gilead's Biktarvy (bictegravir 50 mg/emtricitabine 200 mg/tenofovir alafenamide 25 mg tablets, B/F/TAF) shows promise as long-term treatment option for PWH who may also have common comorbidities or other health needs, according to researchers presenting phase 3 data at CROI. PWH with hepatitis B (HBV) and tuberculosis (TB) coinfection have complex and changing treatment needs. ALLIANCE (NCT03547908) is **the first randomized clinical trial of TAF- versus TDF-based regimens in treatment-naïve adults with HIV and HBV**. Previously reported week 96 results demonstrated the efficacy of both antiretroviral regimens. Data presented at CROI further investigated the factors associated with the HBV treatment response observed with Biktarvy compared to DTG+F/TDF. This subgroup analysis showed that "TAF- versus TDF-based therapy for many HBV treatment outcomes may be greater for certain subgroups, supporting the continued evaluation of Biktarvy in this population." Subgroups showing a favorable response to Biktarvy included younger people and "those with certain levels or types of HBV DNA/genotypes and those with higher-than-normal liver enzymes, among others."

In addition, researchers at CROI also presented week 24 data from the INSIGHT (NCT04734652) trial evaluating Biktarvy in people with HIV and tuberculosis, which is significant because TB is the leading cause of death globally for PWH. In a subgroup analysis comparing participants on Biktarvy compared to individuals on DTG+F/TDF showed that 97% percent of participants treated with Biktarvy achieved viral suppression as did 97% of individuals treated with the DTG-based regimen. "Serious adverse events (AEs) were common in this population with advanced HIV disease and TB, however, none of the reported AEs were deemed related to the study drug."

BEING BRIDGETTE
Bridgette Picou

Trust in medication or in medication we trust?

People may sometimes confuse trust with faith, which is understandable since they feel similar when you process them in daily life. For context, faith is a belief system and trust is an action. To a certain degree, we place a little bit of both in our HIV medications every time we take them. We trust that the medication is going to do what it is supposed to when we take it and have faith that it will keep us healthy.

Clinicians and healthcare providers play a big, but understated, role in whether people take their medications for HIV. They can influence if a person chooses to try a new HIV medication or intervention, like switching from an oral pill to an injectable medication. They will also guide how trust, once lost, is rebuilt, such as in the case of a treatment failure. Undetectable equals untransmittable—or U=U—is another area where we rely on medications to work. Trust is predicated on factors of logic, authenticity or believability and a willingness to act on those factors. For people taking or starting HIV meds, it's the willingness to act that counts.

As HIV medications have evolved over the years, so has the way we look at them. What was once desperation for solutions to stay alive has now become varied, almost casual, and preferential choices. When AZT first came on the market, people took it despite all the harmful side effects and its visible failure rate. Whether that was an act of trust, a leap of faith, or simple hope is up for individual interpretation.

The relationship a person has (or doesn't have) with a care provider can influence the decision to take medication. Considering the power dynamics that usually exist between a patient and clinician, some amount of trust plays into the decision to follow a plan of care. Proximity to privilege is a big factor in trust. This plays out in things like socio-economic status, access to care, representation in identity and culture, and the frequency in which a person had healthcare *before* an HIV diagnosis, these are factors in what trust looks like for them.

Think in terms of *rapid start*. An HIV diagnosis might be a person's first time seeing a provider; they've just had a life-changing event, and they're expected to start taking a medication, potentially for the rest of their life—all within hours? A person has to trust in something for that to be doable. Even outside of rapid start, the choice to begin HIV treatment can be a matter of what you *don't know* against how much you *need to know* to make a choice. Ciarra "Ci Ci" Covin, a Black HIV advocate, says "I trusted my doctor more [than the medication] because I trusted the science. I trusted that my doctor would be knowledgeable enough to translate the science." She now uses her platform to help people feel informed and assured in the knowledge about HIV. Historically, Black people have had a complicated relationship with healthcare and medication. For my part, I trusted the medication over my clinician and in what I was able to parse together about how the medication worked because I didn't feel supported or heard by my first HIV doctor. What I knew at that point was that I wanted to live and feel some version of normal, and ostensibly the medication would make that happen.

We have to remember as well that sometimes, taking medication doesn't just affect the individual. For example, because infant prophylaxis is "standard of care", and often standards of care remove choice, or the idea of having a choice, when women become pregnant and have children, they have to reconcile decisions about whether or not they trust the medication to keep their babies HIV-negative against potential toxicity and side effects. This may also become a larger conversation involving their partners or immediate family. I asked Heather O'Conner, a mother and openly positive advocate who has had two HIV-negative children that she breastfed how trust factored into her kids taking ART (anti-retroviral therapy) after they were born. She says in part "With my children, I trusted my doctor much more. Giving the medication to them was a difficult decision to make, but I was reassured time and time again by my provider that the benefits of my breastmilk outweighed any potential side effects that the medication would cause ... If given the chance again, I'm not sure I would have my children on the medication, although they presented with no side effects other than temporary gastrointestinal upset and a brief period where they teetered on the edge of slight anemia." She says her husband felt good about the assurances from the doctor, but also held trust in her as a mother. The underlying faith in pregnancy is that medications and undetectable status will prevent transmission of HIV from mother to child.

As medication delivery modalities change, information about drugs and how they work must remain readily accessible and understandable. Clinicians involved in HIV have to remember how important a patient's trust is in either the care provider themselves or in the medication they are prescribed. Trust given is not trust so easily rebuilt once lost.

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