POSITIVELY AWARE

MARCH+APRIL 2023

YOUR TICKET

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

THE 27TH ANNUAL HIV DRUG GUIDE

OUT AND ABOUT

The private journey to being seen

'PH

ar

POSITIVELY AWARE

For pagination purposes, this page has been intentionally left blank.

PHOTO:

POSITIVELY AWARE

For pagination purposes, this page has been intentionally left blank.

PHOTO:

POSITIVELY AWARE

LIVE LIFE POSITIVELY AWARE.
SINCE 1990, PUBLISHED BY
TPAN
5537 N. BROADWAY
CHICAGO, IL 60640-1405
(773) 989-9400
FAX: (773) 989-9494
inbox@positivelyaware.com
positivelyaware.com
@PosAware

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

BE GREEN.
SHARE OR RECYCLE
THIS MAGAZINE.

THE 27TH ANNUAL HIV DRUG GUIDE

MARCH+APRIL 2023

POSITIVELY AWARE • VOLUME 33 NUMBER 2 • positivelyaware.com • @posaware

EVERY ISSUE

'Allow yourself to be loved. There is life after diagnosis. If you claim it.'

—**SANFORD E. GAYLORD**, ON WHAT HE WOULD TELL HIS YOUNGER SELF, TAKING PART IN THE COVER PHOTO SHOOT FOR THE FIRST POSITIVELY AWARE HIV DRUG GUIDE, IN 1997.
PAGE 75

THIS ISSUE

THE 27TH ANNUAL HIV DRUG GUIDE

SEE AND BE SEEN:
FROM LEFT: D'ONTACE KEYES, DANI KRUSE, JUDY BROWN, ACES LIRA, TIMOTHY S. JACKSON, COLEMAN 'BOY COLE' GOODE, NIRMALPAL SACHDEV AND JOEL B. COHEN

'Out' in the open

The private journey to being seen as a person living with HIV

STORY BY **RICK GUASCO** · PHOTOGRAPHY BY **JOHN GRESS** · STYLING BY **WILLIAM MARTINEZ**

For **Aces Lira**, 29, taking part in the cover photo shoot of the **27th annual POSITIVELY AWARE HIV Drug Guide** was the next milestone in his journey while finding connection with other people living with HIV.

"The timing felt right," he said. "I knew doing this, I would connect with other people living openly about their experiences with HIV."

Lira was excited at the opportunity to share his story and find community that he invited a couple friends to join him. While they weren't ready as he was to go in front of the camera, they wanted to show their support, meeting him at The Baton Show Lounge, an iconic drag show venue in Chicago's Uptown neighborhood, the location of the photo shoot.

"I myself was diagnosed two years ago," said Lira's friend Kyle. "I just came to show support and let him know that I was happy that he was confident enough to display in public that he's positive. I don't think I'm there yet in my journey to do that. Admiring and supporting him really is why I came."

Another friend, Qiana, was also on hand. "I think it's pretty huge, what he's doing and I'm just very proud of him to be at this point in his journey," she said.

"Even if the public doesn't see them photographed, their love and support are still in the photos," Lira said. "It helped having my friends physically present. While we waited for direction and set-ups, we would giggle together and meet with the others in the shoot. It's not often I get to meet and create friendships with other people living with HIV, and so I hold them in high regard. It meant everything to me having them there supporting me and enjoying themselves."

For Lira, the photo shoot was a chance to socialize and even network. "The lightbulb went off for me during the shoot," he said. "I realized we need moments to connect with one another more often. We might be living with HIV but we deserve to be humanized and be seen. We do what we can to create a support system, but the number of folks who are open about their status runs small. I wanted to introduce my friends to each other and this was an opportunity. They got to also meet other folks to exchange contact info and talk about projects they're working on. I think at one point there was an informal support group

sharing experiences with one another talking about changes to treatment over time and what brought us all here."

A policy and advocacy manager for an HIV organization in Chicago, he reflected on his six years living with HIV. "It's been a bittersweet experience," he said. "On one end, my diagnosis created a window to meet incredibly inspiring people trying to make a difference for people vulnerable or living with HIV. On the other, it's been years of breaking through feelings of shame and isolation when I was first diagnosed. I can still remember the few friends I reached out to when I first found out and the support and love they gave me helped anchor me. That's reason enough for us to be open about our experiences and support one another when we need it."

Judy Brown finds support groups have been a vital part of living with HIV. At 72, Brown has been living with HIV for 30 years.

"Support groups have been key to my staying strong; they are a safe space," she said. "That's why I love to help run and facilitate support groups. I've met a lot of amazing people who I probably would not know if I wasn't living with HIV. So, I look at it in that light. I've learned a lot from other people."

Having a vision and a purpose are important to Brown. "I love advocacy work, especially to empower all women," she said. "My vision was to live after my diagnosis in my forties. I think I've come a long way. I'm happy and proud."

Nirmalpal Sachdev, 49, is proud of his 26 years living with HIV so far. "After receiving my diagnosis at 23 I thought my life was over," he said. "Over the years, as medications improved, I have come to terms with my HIV status as a chronic illness that reminds me to take care of my health. Having to self-disclose to those I am intimate with about my status humbled me at such a young age. Having HIV reminded me that real good people are usually unafraid and accepting. I'm glad to have learned that lesson at such a young age."

His desire to be a visible example of a long-term survivor motivated Sachdev to take part in the cover shoot. "I am living proof that having this virus inside me for over 25 years and taking a long, long, long list of various medications over the years hasn't changed my appearance or my desire to live," he said. "I think it's important for those who are newly diagnosed, and those wondering what they will look like after years of medication, to see someone like me who's had it for so long and still looks as sexy as ever. You just gotta keep going."

For someone who is newly diagnosed, he offered this advice: "Take a deep breath. "Feel all the feels. Accept the range of emotions. Get angry if you need to, and then start looking for support. We are all here for you. You are not alone."

Coleman "Boy Cole" Goode came to The Baton dressed to make more than just a fashion statement. "I believe that representation matters, we need to see ourselves reflected in positive imagery," he said. "It's why I chose to be photographed in leather to represent all of those Leatherfolk who have come before and will come after me."

The 42-year-old community organizer has been living with HIV for 17 years. "I live a life today where the only time I think about my HIV is when I take my meds," he said. "HIV does not control my life because I'm more than someone living with HIV today."

He added, "HIV is no longer a death sentence; medications have come a long way, and you will have a life beyond your wildest dreams."

At about the same time **Joel B. Cohen**, 72, was diagnosed with HIV 27 years ago, he learned he had early-onset Parkinson's disease (PD). An economist for 40 years, Cohen changed careers and became a social worker in 2019. He credits his rigorous exercise routine—and the demands of fatherhood—for his good health.

"I'm not trying to minimize the seriousness of HIV, but some things in my life need to yield to the demands in my life," he said. "My T cell count was down to seven, but by the end of the first week following my diagnosis and hospitalization, I resumed taking solo care of my two school-age children. By the end of the fourth week following my diagnosis, I returned to work full-time. Stepping up my exercise routine—including sneaking in multiple sets of pushups during my days in the office—has not only slowed or halted the progression of PD, but has reversed it. About HIV, all I do is pop a pill once a day and continue following healthy habits—pretty simple in comparison to dealing with PD."

Cohen pushed himself to do the photo shoot. "I have a tendency to isolate myself as I deal with issues surrounding my own health and my family," he said. "I realize that others react pretty much the same as I do, and my participation contributes to the understanding, knowledge and feeling that none of us are alone or need to be alone. The strength offered by the HIV community benefits everyone."

Appearing on the cover of the drug guide, **Timothy S. Jackson** has come full circle.

"When I was newly diagnosed, I often flipped through the pages of Positively Aware, absolutely amazed at the bravery of people living with HIV sharing their story," he said. "Seeing those advocates standing firmly in their truth unabashed by HIV-related stigma, it gave me the courage to do the same. My participation in the photo shoot will hopefully inspire someone newly diagnosed to take the same steps I did to beat back stigma."

Jackson, 41, is the director of government relations for AIDS Foundation Chicago and has been living with HIV for 13 years. "As a Black gay man living with HIV, my life is deeply rooted in advocating on behalf of people living with HIV and amplifying the voices of the communities where my identities intersect."

He shared what he would tell someone who is newly diagnosed. "First, I would tell them to breathe and that it will be O.K. . Secondly, I would tell them that they are loved and deserve to be loved. Finally, I would encourage them, if able, to find a network of people living with HIV to help cope with this new normal."

Anyone can have HIV; **Dani Kruse** points to herself as an example. The owner of a catering and staffing company, she describes herself as "a white woman from Iowa." Kruse had been "really sick for several years" with an inexplicable ailment. No one (including herself) had thought to test for HIV. She was diagnosed with AIDS in 2016. With only 10 T cells, doctors estimated she must have been living with untreated HIV for 12–20 years.

"I chose to be in this photo shoot because anyone can have HIV—including white, middle-aged women from small towns," Kruse said. "I believe the only way to reduce the spread of this disease (virus really) is through education and ending stigma."

She reflected on her life since diagnosis. "HIV changes your life, but does not change who you are. I was health conscious prior to my diagnosis, but I learned so much about the importance of sleep, the need for having a 'village'—I have some amazing friends in my village, including two pug puppies.

"I learned that I am an amazing kickass human being; you are, too," she added. "Learn, become self-forgiving, give yourself a break. HIV is not as big as it might seem."

D. Dontace Keyes, 33, has spent the last 15 years "adapting to HIV," as he described it. "I've just begun living. This is my life, and I don't give a damn about lost emotions. I've such a lot of love I've got to give; let me live."

He was moved to join the photo shoot for the people in his life. "For my tribe of mothers, sistas and village of brothers who ever wondered, *what will happen to all that beauty?*" he said. "It's living and giving." PA

THE COVER and the pictures from this series were photographed by **John Gress** and styled by **William Martinez**.

Losing ground

During the COVID-19 pandemic, local basic HIV programs were halted, and many support groups never came back. Bureaucratic and logistical red tape have slowed lifesaving HIV programs. Peer navigation roles to reach the most vulnerable are few and far in between; funding tends to flow to well-established organizations that may crowd a community group offering the same type of service. It took me three months to have pharmacies accept standard ADAP paperwork, so I had a stockpile of supplies. I have seen offices and agencies where stigma and discrimination are fanned by anti-LGBTQ+ messaging from elected officials, but pointing out structural problems can get people labeled as "woke."

I am worried that HIV outcomes look better on paper than in real life. What works well in public health plans doesn't necessarily play out in the field. Without meaningfully involving the PLWH [people living with HIV] community and political will, we may lose what progress we've gained because the resources are no longer there.

—ANTHONY ADERO
WASHINGTON, D.C.

Published poet

Surprise!!! It's official, *I'm a published poet!* Thank you, @posaware, for featuring my poetry! My baby, *Iridescent*, is in the universe! This is for my transgender community worldwide. Feel, heal, and enjoy! Check out *Iridescent*, on page 27 in the January+February 2023 issue.

—@TIMELESSTATE ON INSTAGRAM

Partners in research

A couple researchers took note of Partners in Research, *our four-part series about long-term survivors of HIV taking part in HIV cure research, which debuted in the January+February issue.*

...it's really good, engaging and well written. Also, I learned some things, including that we should think about flu/COVID season for a start. And definitely the need for follow-up for participants after ATIs [analytical treatment interruptions]. Congratulations to everyone involved in putting this together.

—PAULA CANNON, PHD
KECK SCHOOL OF MEDICINE,
UNIVERSITY OF SOUTHERN
CALIFORNIA

It offers reasons for the need for participants and provides firsthand knowledge of the experience of being involved in cure research. Important work like this will help increase participation and open stories to the rest of the world about HIV cure research. I am inspired. Well done!

—PAULINE SAMESHIMA, PHD
GRADUATE STUDIES AND RESEARCH
IN EDUCATION
LAKEHEAD UNIVERSITY

©2023 POSITIVELY AWARE (ISSN: 1523-2883) is published bi-monthly by Test Positive Aware Network (TPAN), 5537 N. Broadway, Chicago, IL 60640. TPAN is an Illinois not-for-profit corporation, providing information and support to anyone concerned with HIV and AIDS issues. POSITIVELY AWARE is a registered trademark of TPAN. All rights reserved. Readership: 100,000. For reprint permission, email inbox@tpan.com. Six issues mailed bulk rate for $30 donation; mailed free to people living with HIV or who are unable to contribute.

NOTE FROM THE ACTING EDITOR-IN-CHIEF

Rick Guasco
@rickguasco

Living from one breakthrough to the next

I'll never forget the first time I disclosed my HIV status. I told my best friend, Jim. He'd known something was up; the growing number of Kaposi sarcoma lesions on my face and body did not go unnoticed. He looked at me for a moment.

"Well, at least you know what you have to do now," Jim said resolutely. "Your strategy is to be here long enough for the next breakthrough, and then use that to make it to the breakthrough after that. And just keep going."

He'd always been a pessimist, so for Jim to say that was extraordinary. It was an act of love and hope. It was 1993, and the only treatment at the time was a drug called azidothymidine, or zidovudine, infamously known as AZT. How far we've come since then.

Our annual HIV Drug Guide (now in its 27th year!) is a handbook of these breakthroughs and what you should know to make the most of them. Pharmacist Eric K. Farmer and associate editor Enid Vázquez have put together an extensive drug-by-drug compendium with insightful comments by HIV specialist Melanie Thompson, MD, and long-term HIV activist and service provider Joey Wynn. Eric has also written the lead article (page 13) about how your "ph-riendly" neighborhood pharmacist can be a valuable resource for your HIV care.

Also helping to make this year's Drug Guide possible are Carla Blieden, PharmD, MPH, AAHIVP, and several of her pharmacy students, who reviewed and contributed to our expanded DHHS recommendations in addition to the drug pages. Olivia G. Ford wrote how updated infant feeding guidelines are helping parents living with HIV. In her column, Bridgette Picou talks about the "D" word—*disclosure*. And special appreciation to art director Greg Mytych, who designs the magazine.

So, how soon will we have a cure? That's probably the question I get asked the most. Not tomorrow. We keep discovering how clever and complicated HIV is. An HIV researcher and two treatment activists have adapted their presentations for the Drug Guide. Dr. Jared Stern explains how HIV works using a cookbook for a metaphor and recalling an episode of the TV series, *Friends* (page 22). Lynda Dee and Jeff Taylor talk about the different strategies that could lead to a cure (page 71).

Advances in HIV treatment are only truly successful when they reach *all* the people who need them. Health equity is the ultimate breakthrough. It's the only way we'll put a stop to this virus. Progress is defined not only by expanding medical knowledge, but by expanding access for *everyone*.

A breakthrough is the culmination of often hard-fought knowledge. It's a gamechanger, but maybe most important, it offers hope. From one breakthrough to the next.

You are not alone.

P.S. POSITIVELY AWARE has a breakthrough of its own this year. In addition to the wall-size and Pocket Edition HIV drug charts, we've introduced the HIV Drug Chart Pocket Edition in Spanish. We hope you share this news with everyone who needs it. Order your charts, in single or bulk orders; **GO TO** positivelyaware.com/order.

PD: Por primera vez, la Tabla de Medicamentos para VIH de POSITIVELY AWARE Edición de Bolsillo está disponible en español. Esperamos que compartas esta noticia con todos los que lo necesiten. **VISITE** la pagina web positivelyaware.com/order.

Advances in HIV treatment are only truly successful when they reach *all* the people who need them. Health equity is the ultimate breakthrough.

JOHN GRESS · ILLUSTRATION: ISTOCK

CONTRIBUTORS

THE EDUCATOR

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 57-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. Wynn 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. Enid's sister Sylvia appeared on the cover of the first drug guide (see page 74—Enid wants to point out that her sister is a fantastic artist). Enid wrote about their long-term survival relationship in the November + December 2016 issue ("Sister, Sister").

THE PHARMACIST

Carla Blieden, PharmD, MPH, AAHIVP, and several of her pharmacy students updated the drug pages and reviewed the Department of Health and Human Services (DHHS) 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. She worked closely with City of Los Angeles officials and the Los Angeles Fire Department on deployment of the influenza and COVID vaccinations. Dr. Blieden is Assistant Professor of Clinical Pharmacy and Director of Student Outreach and Community Health at the USC School of Pharmacy.

FARMER AND VÁZQUEZ: JOHN GRESS • BLIEDEN: ISAAC MORA

Want to stay undetectable* with fewer medicines?

detect this.

Ann
Retired Educator & Author
Switched to DOVATO
Compensated by ViiV Healthcare

Dovato
dolutegravir 50 mg/
lamivudine 300 mg tablets

Results may vary.
*Undetectable means the amount of HIV in your blood is below the level that can be measured by a lab test.
†Compared to a 3- or 4-drug regimen.

No other complete HIV pill uses fewer medicines to help keep you undetectable.†

DOVATO is different: unlike other HIV treatments that contain 3 or 4 medicines, DOVATO contains just 2 medicines in 1 pill.

DOVATO is a complete prescription regimen for adults new to HIV-1 treatment or replacing their current HIV-1 regimen when their doctor determines they meet certain requirements.

Learn more at **DOVATO.com**

Important Facts About DOVATO

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

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

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

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

For more information about side effects, see "What are possible side effects of DOVATO?"

What is DOVATO?

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

Please see additional Important Facts About DOVATO on the following page.

Ask your doctor about staying undetectable with fewer medicines in 1 pill.

Dovato
dolutegravir 50 mg/
lamivudine 300 mg tablets

Important Facts About DOVATO (cont'd)

Who should not take DOVATO?

Do not take DOVATO if you:

- have ever had an allergic reaction to a medicine that contains dolutegravir or lamivudine.
- take dofetilide. Taking DOVATO and dofetilide can cause side effects that may be serious or life-threatening.

What should I tell my healthcare provider before using DOVATO?

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

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

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

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

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

What are possible side effects of DOVATO?

DOVATO can cause serious side effects, including:

- See **"What is the most important information I should know about DOVATO?"**

What are possible side effects of DOVATO? (cont'd)

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

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

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

Where can I find more information?

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

October 2022 DVT:7PIL

THE CATEGORY IS

JOY

Living with HIV, we are more than our diagnosis. If you're living with HIV, *what gives you joy?*

We asked our social media followers, and they responded
COMPILED BY **RICK GUASCO**

"Self-love and my children, my grandchildren and my great-grandchildren. Life gives me joy; having a God that loves me unconditionally. Family, friends and my church family."
—ANGELA COPELAND

"HIV led me to counseling, which in turn prodded me into getting my BS in psychology and counseling men and women with HIV, and also doing some palliative care."
—BRUCE FOURNIER

"My doggies, Andy, Mario and Onix!"
—WILLIAM TORRES, HIV SOCIAL WORKER AND ADVOCATE

"Being able to continue being an advocate on HIV, aging, homelessness, food insecurity and related issues. Coming back from significant health issues the past couple years, I'm living out loud so that others gain encouragement."
—WANDA BRENDLE-MOSS

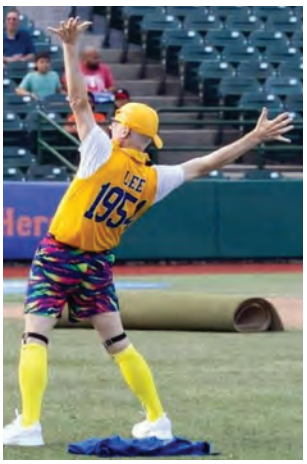
"People who accept you for who you are. People who genuinely care about people."
—JOHN ZEE

"First, knowing I have HIV; HIV don't have me. It brings me great joy when people reach out to me for help. That increases my faith in what God told me and shows me. He said that all my pain, sadness and everything I was going through mentally and in my life wasn't for nothing. My pain would help others. That brings me a lot of joy, knowing that things I've experienced and healed from, I now use to help others living with and affected by HIV. It brings me much joy knowing that HIV don't stop nothing in my life. Not just HIV, but abuse, anxiety, depression, stress and life in general. I get joy knowing that God is with me and has chosen me for something amazing. God turned it around and it's now helping create hope for people suffering in silence. I get joy every day when I open my eyes knowing I am alive, while living a life on a forever healing journey. I get joy seeing hurt people heal, then help people. We are changing the narrative."
—CHATRIVIA KENNEDY

—LAURIE ANN

"Warm days, fresh flowers, my nieces and nephews, and good friends."
—KATRINA BALOVLENKOV

"Solitude, food and movies."
—JAMES BRADFORD



"Dancing and performing. Last year I joined a senior citizen dance team, The Pacemakers. I'm having a blast!"
—LEE RAINES

"Thirty-eight years and still going strong, now living my dream of living by the ocean."
—GREG KNEPPER

"Giving back brings me joy. Even though from the very beginning of my testing positive I lived every day with the attitude *this is what I have, it does not define me.* Through a recent path that led me to becoming a certified recovery coach, it's given me the opportunity to give back to all walks of life. A joy I thought I'd never find."
—KATE ELLING

ILLUSTRATION: DENIS NOVIKOV/ISTOCK

Ask your 'ph-riendly' neighborhood pharmacist

A pharmacist does more than fill your prescription; they are a resource who can help get you more engaged in care

BY **ERIC K. FARMER, PharMD, BCPS, AAHIVP**

After nearly four decades of HIV research and medical advancements, more novel medications are available for managing HIV than ever before. Despite this, the same basic principle of HIV therapy remains true: successful treatment and subsequent positive outcomes require engagement in care and good adherence to HIV medicines.

While HIV providers with all different types of credentials may continue to chant the mantra "Take your medicines" at every appointment, it remains difficult for some individuals. Given the strong data showing modern-day HIV medicine combinations work, any detectable viral load likely indicates a degree of incomplete adherence.[1]

Enter the pharmacist

When was the last time you talked to your pharmacist? Whether it is at the pharmacy down the street, at the doctor's office or in the hospital, pharmacists are involved in providing care to people with HIV. More than 90% of people in the United States who live in urban areas are within two miles of a pharmacy and about 70% who live in rural areas are within 15 miles of one.[2,3] Pharmacists are some of the most accessible health care providers, usually practicing in the community or settings where they regularly interact with patients and the general public. Pharmacies are non-stigmatizing venues in the community where individuals can do more than just pick up medications. In addition to just dispensing medications, pharmacies are now places where you can go to get vaccines, get information about your medications, get screened for various diseases and conditions, ask questions about your healthcare and much more.[4]

All in a day's work for a pharmacist

Pharmacists are uniquely positioned throughout the healthcare system to support and focus on several aspects of care specifically relating to medications, such as regularly assessing adherence to HIV medication or evaluating a patient's barriers to care. Pharmacists may routinely connect with a patient, developing a strong rapport and thus helping to keep them engaged in care. They may also be aware of and assist with referring you to community resources or other professionals who may further support your goals of care.[5]

Before you pick up your prescription at the pharmacy, a lot of work was done behind the scenes to ensure that medication is safe and effective for you. A pharmacist's involvement may have included, but is not limited to, making sure it is the correct drug, dose, directions, reviewing your drug resistance profile, possible side effects, medication-related allergies and cost, as well as evaluating for any possible drug interactions. HIV medications have many drug interactions with other medicines, vitamins, supplements, herbal products, recreational substances and more, so it is important to discuss all medicines, including over-the-counter products you take, with the pharmacist.[5] **SEE TABLE 1** on page 14 for a list of common over-the-counter, herbal and recreational substances that have significant interactions with some HIV medications.

Reducing disparities

Pharmacists' drug knowledge expertise paired with their relative accessibility to patients and providers will be essential to addressing healthcare disparities and expanding access to HIV treatment initiatives as new drug therapies continue to become available. By recognizing their expanding role in managing HIV and by including them as essential members of the healthcare team, pharmacists can become another advocate for promoting the pillars of the federal Ending the HIV Epidemic (EHE) Initiative and ultimately the goal of achieving and maintaining a suppressed viral load, preventing the spread of HIV, and ending the epidemic.[4]

Working with your pharmacist

Even if you don't see your pharmacist every visit, there are several things you can do to be better prepared to discuss your medications and medication concerns with your healthcare providers.

According to the Institute for Safe Medication Practices, one of the "Key Elements of Safe Medication Use" is patient education. Patients should receive ongoing education from physicians, pharmacists and other healthcare team members about the medications they are receiving, their indications (what the medication is for), dose(s), possible side effects, drug or food interactions, and how to protect themselves from potential errors.

"Patients can play a vital role in preventing medication errors when they have been encouraged to ask questions and seek answers about their medications before drugs are dispensed at a pharmacy or administered in a hospital," the institute noted in its report.[6]

The importance of shared decision making between the patient and their provider(s) in the current era of HIV management cannot be overstated. **SEE TABLE 2** on page 14 for a list of ways you can be better engaged with your healthcare team about medications. Go to your medical appointment feeling empowered and prepared. PA

GO TO positivelyaware.com **for the footnoted references in this article.**

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.

ISTOCK

Common over-the-counter vitamins, supplements, herbal products and recreational substances that can have

Supplement	HIV medication interaction
Multivitamins and "Multi-valent cations" (vitamins that contain elements and minerals such as iron, calcium, magnesium, zinc, aluminum or other similar elements)	If taken at the same time on an empty stomach, **vitamins and supplements such as iron and calcium can bind to integrase inhibitors (e.g., bictegravir, dolutegravir, elvitegravir, raltegravir) like magnets and significantly decrease absorption.** A lower concentration of HIV medication can lead to treatment failure and resistance. This does not apply to medications that are injected (like cabotegravir). In general, **it's O.K. to take vitamins and supplements at the same time as your HIV meds with food**. You can also **take HIV medication 2 hours before or 6 hours after taking a vitamin**. Regardless of food, **it is not recommended to take Isentress with aluminum- or magnesium-containing supplements.**
Red yeast rice (used for cholesterol)	Red yeast rice contains monacolin K, a natural component with the same chemical structure as lovastatin. Coadministration of lovastatin with HIV medicines containing a boosting agent or a protease inhibitor can result in potentially serious reactions such as myopathy (muscle aches) or rhabdomyolysis (a severe breakdown of muscle tissue usually requiring hospitalization or close medical monitoring). **It is recommended to use an alternative medicine for cholesterol if needed.**
St. John's Wort (used for depression)	St. John's Wort is expected to substantially decrease concentrations of most HIV medicines. A lower concentration of HIV medication can lead to treatment failure and resistance. **It is recommended to use an alternative medicine for depression if needed.**
Acid-suppressing medications (used for heartburn or gastro-esophageal reflux disease, GERD) in antacids such as Tums, Pepto-Bismol, Mylanta or Maalox; H2 blockers like cimetidine, famotidine or ranitidine; and proton pump inhibitors like dexlansoprazole, esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole.	**Drugs that lower stomach acid can significantly decrease the absorption of some HIV medications like rilpivirine or atazanavir.** Lower concentrations of HIV medication can lead to treatment failure and resistance. ***HIV medications containing rilpivirine or atazanavir should always be taken with food. It is recommended to take antacids 2 hours before or at least 4 hours after HIV medicines containing rilpivirine.*** *Generally,* ***it is recommended to take H2 blockers 12 hours before or at least 4 hours after HIV medicines containing rilpivirine.*** *It is* ***not*** ***recommended to take proton pump inhibitors with any oral HIV medicines containing rilpivirine.*** *It is recommended to take HIV medicines containing atazanavir 2 hours before or 1 hour after antacids.* Depending on the dose of atazanavir and other drug interactions present, there is specific guidance for administration of H2 blockers and proton pump inhibitors contained in the prescribing information.
Contraceptives (used for birth control)	Coadministration of some HIV medicines containing protease inhibitors (e.g. darunavir or atazanavir) or non-nucleoside reverse transcriptase inhibitors (e.g., efavirenz, etravirine, or nevirapine) with hormones used for contraception may decrease hormone levels and decrease their effectiveness. ***It is recommended to use different HIV medicines or alternative/back up contraceptive methods.***

significant interactions with HIV medications [*1,7]

Supplement	HIV medication interaction
Inhaled corticosteroids (used for allergies or asthma) such as budesonide, ciclesonide, fluticasone or mometasone in products like Advair, Arnuity Ellipta, Asmanex, Breo Ellipta, Dulera, Flonase, Nasonex, Symbicort or Trelegy Ellipta	Regular or daily coadministration of any over-the-counter or prescription inhaled or nasal spray corticosteroids with an HIV medicine containing **a boosting agent such as cobicistat or ritonavir or a protease inhibitor can significantly increase the steroid concentration.** This interaction can increase the risk for Cushing's syndrome and adrenal suppression as well as other complications. ***An alternative steroid that does not have a strong interaction is recommended.***
Phosphodiesterase 5 (PDE-5) inhibitors (used for erectile dysfunction or heart failure) such as sildenafil, tadalafil or vardenafil in products like Cialis, Levitra, or Viagra	Coadministration of HIV medicines containing **a boosting agent such as cobicistat or ritonavir or a protease inhibitor can significantly increase the PDE-5 inhibitor concentration.** This interaction can lead to complications such as significantly low blood pressure, vision changes, and a prolonged painful erection called priapism. Depending on the PDE-5 inhibitor being used, there is specific guidance for coadministration contained in the prescribing information.
Methamphetamines	Coadministration of HIV medicines containing **a boosting agent such as cobicistat or ritonavir or a protease inhibitor can significantly increase methamphetamine concentrations.** This increases the risk of overdose. Because the concentration of methamphetamine and a person's tolerance to the substance can be variable, it is important to use with caution and be sure someone nearby is sober who can be trusted to call for help if needed. Consider discussing changing HIV medicines to minimize interaction.
Cocaine	Coadministration of HIV medicines containing **a boosting agent such as cobicistat or ritonavir or a protease inhibitor can increase cocaine concentrations.** This increases the effects of cocaine and may increase the risk of heart attack, stroke or seizures. Because the concentration of cocaine and an individual's tolerance to the substance can vary, it's important to use cautiously and be sure someone nearby is sober who can be trusted to call for help if needed. Consider discussing changing HIV medicines to minimize interaction.
Ecstasy, X, MDMA	Coadministration of HIV medicines containing **a boosting agent such as cobicistat or ritonavir or a protease inhibitor can significantly increase MDMA concentrations**. This increases the effects of MDMA, such as rising heart rate and blood pressure as well as increasing the risk of dehydration. Because individual reactions to MDMA can vary, it's important to use cautiously and be sure someone nearby is sober who can be trusted to call for help if needed. May also discuss changing HIV medicines to minimize interaction.

***This is not a complete list of interactions.** Descriptions of interactions listed are only generalizations and are not meant to be used in place of clinical judgement. It is recommended all medications be evaluated for possible drug interactions prior to administration per patient and discussed with your provider(s).

Strategies to enhance discussions about medications with your healthcare providers

✓	Bring a list of all active medications with you to every appointment and review with your provider(s).
	Be sure to list and discuss all over-the-counter medications, herbals, supplements, vitamins, minerals, nasal sprays, inhalers, eye drops, ear drops, topical products and recreational substances with your provider(s) including your pharmacist to check for drug interactions.
	Ask your provider(s) or pharmacist about possible drug interactions with a new medication or over-the-counter supplement ***before*** you take it.
	Bring a list of all providers and specialists with you to every appointment and keep track of when your next appointments are scheduled.
	Keep a list or journal of any side effects, concerns or questions you have and talk about them with your provider(s) at your appointment.
	Research your health condition(s) and write down any questions to ask your provider(s).
	Review your lab results; write down any questions to ask your provider(s).
	Be sure to note and communicate with your provider(s) any time you start or stop a new medication.
	Note and discuss any specific goals or barriers to care at every appointment.
	Let your provider(s) know if you are having difficulty affording your HIV medication. Your provider(s) cannot help you if they do not know there is a problem.
	Be sure your address, contact information and emergency contacts are updated at each provider appointment.
	Request community resources or credible websites to find more information and support about your health condition(s).
	For some appointments, it may be helpful to bring all your medicines and/or medicine bottles to your appointment.
	Try to minimize the number of pharmacies you use. This will help coordinate refills as well as will ensure all new medications are checked in the same database for any possible drug interactions. Not all pharmacy systems are linked.
	Bring all active and available insurance information with you to every provider appointment and to the pharmacy, even if they don't usually ask for it or if you think they already have it.

Provider resources

DHHS Guidelines for Use of Antiretroviral Agents in Adults and Adolescents
clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv

University of Liverpool HIV Drug Interactions
hiv-druginteractions.org

AIDS Education & Training Centers
aidsetc.org

Clinical Care Options HIV
clinicalcareoptions.com/HIV.aspx

Patient resources

Centers for Disease Control and Prevention
cdc.gov/hiv

The Body
thebody.com

POSITIVELY AWARE
positivelyaware.com

National AIDS Treatment Advocacy Project
natap.org

POSITIVELY AWARE

For pagination purposes, this page has been intentionally left blank.

PHOTO:

Infant feeding

How updated guidelines help parents living with HIV

BY **OLIVIA G. FORD**

Infant-feeding for parents living with HIV in the U.S. has improved tremendously with updated federal guidance that now affirms informed, shared decision-making.

In late January, a panel of experts in perinatal HIV treatment, care and prevention, in consultation with community advocates and pediatric experts, revised the "Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States"—often known as the Perinatal HIV Clinical Guidelines—issued by the U.S. Department of Health and Human Services (DHHS). The update reflects what has already been the standard of perinatal HIV care for most of the world: Breast/chestfeeding can be a safe, healthy option for virally suppressed parents with HIV and their babies. Further, there are infant-feeding considerations beyond the (low) possibility of HIV transmission.

National medical associations such as the American Academy of Pediatrics are expected to make similar updates, and the U.S. Centers for Disease Control and Prevention (CDC) has committed to referring to these guidelines rather than maintaining separate recommendations.

Here are five key entry points about infant-feeding and the updated Perinatal HIV Clinical Guidelines.

1 The chance of breast milk HIV transmission from a parent taking HIV treatment is very low.

The updated guidelines clarify what we have learned from studies in resource-limited regions: effective HIV treatment and undetectable viral load for lactating parents drives babies' likelihood of acquiring HIV during breast/chestfeeding below 1%.

In recent years, guidelines in high-resource countries like the U.S. have included language around supporting parents who choose to breastfeed "despite" recommendations against this practice. The current guidelines include no such discouragement. They explain that formula feeding eliminates *any* possibility of HIV transmission, and that a less than 1% chance is not zero. It is worth noting that the likelihood of transmission through pregnancy and birth is also considered to be less than 1%, though technically not zero. Since that initial triumph of treatment as prevention beginning in the 1990s, it has been increasingly well known that with access to prenatal care and HIV medication, babies are born without HIV. Infant HIV acquisition usually signals lack of access to this care.

Does this mean U=U for breast/chestfeeding? Presently, no. We have piles of studies showing unequivocally that there is zero chance of acquiring HIV sexually from a person whose viral load is undetectable. That is not yet the case here—but the pool of data may yet grow and further demonstrate that, with these conditions in place, undetectable does indeed equal untransmittable during breast/chestfeeding.

2 Breastfeeding has benefits for infants and parents.

Clear, copious evidence indicates that breastfeeding—the preferred infant feeding method of the human species—is also the healthiest option for babies and parents who are able to do so. Health benefits highlighted in the newest version of the guidelines, citing CDC literature, include lower rates of sudden infant death syndrome, asthma, obesity, and type 1 diabetes for breastfed infants. Further, breast/chestfeeding parents experience lower rates of hypertension, type 2 diabetes, and several reproductive cancers—in addition to important cultural, emotional, cost-saving, and convenience benefits of feeding one's child from their body.

"I was entirely surprised when I learned the benefits of breastfeeding, including the bonding that happens during this time between mother and child," said Ciarra "Ci Ci" Covin, program manager at The Well Project and an advocate who advised on the guidelines updates, in a recent email conversation.

Like HIV, the aforementioned health conditions disproportionately affect Black parents and babies. Meanwhile, CDC has reported that hospitals serving Black birthing parents are less likely to offer evidence-based maternity care, including encouraging breastfeeding in the crucial first hour of life—and not offering formula unless medically indicated. This is one of many ways systemic racism thwarts Black women's breastfeeding potential—and a key reason behind lower breastfeeding rates among Black parents than any other racial group in the U.S.

In the midst of a maternal and infant mortality crisis in which Black and also indigenous birthing parents and infants are far more likely to die from conditions related to giving birth—or being born—than their White counterparts, this is arguably the community that could benefit from breastfeeding support the most. As the updated guidelines indicate, this context of inequity must be considered as part of counseling and supporting birthing parents with HIV—a high percentage of whom will likely be Black women.

"One thing that really resonated with me while I fed my child from my body, is that I was able to feed my child in the way my ancestors fed theirs," said Covin.

3 Providers should discuss a range of options with parents and support them in their decision.

Covin has given birth to two HIV-negative children while living with HIV, the second of whom she breastfed. "We do not

ISTOCK

need approval; we need support" around infant feeding options, she said. While shared decision-making is an important framework, central to the updated guidelines, ultimately how a parent feeds their baby is their decision. A provider who supports that approach is supporting parents' agency as well as their health.

It's important to note that the guidelines updates are not about getting everyone to breast/chestfeed, but providing information and resources to enable parents to make the best decision for themselves and their families. The updated guidelines advise providers to start infant feeding conversations with a question such as: "Have you thought about how you would like to feed your baby?", and then outline methods of doing so. Offering this information sets a tone of trust in a parent's ability to make an informed decision.

If a parent chooses to formula feed, then support includes ensuring they have access to safe water to mix it (not a given even in the U.S., in this era of water crises in Michigan, Mississippi and elsewhere) and can afford to buy or otherwise access sufficient formula. Screened, pasteurized donor human milk, offered through milk banks with a provider's prescription, may be an intriguing option for some but may not be accessible due to cost, supply or other factors.

Whether breast/chestfeeding or not, a parent's adherence to HIV meds is vital after giving birth to preserve their own health and, if breast/chestfeeding, to prevent infant HIV acquisition. Support is essential to adhere to *anything* during the often confusing, exhausting, sticky, messy, blissful, lonely postpartum period.

Providers may ensure a new parent has the clinical, mental health and support engagement needed to maintain their HIV med regimen—as well as people caring for *them* as they transition into this new phase of life. And like so many other social benefits, the U.S.'s virtually nonexistent postpartum infrastructure (no guaranteed paid parental leave, paltry clinical follow-up, poor access to lactation support, etc.) stands in stark contrast to comparable nations. Even the American College of Obstetricians and Gynecologists has declared the need to strengthen postpartum care. We must do better, for *all* parents of any HIV status.

Calling Child Protective Services does harm—and no good

The child-welfare system in the U.S., put plainly by renowned legal scholar and reproductive justice pioneer Dorothy Roberts in *Time* magazine last year, is "designed to deal with the hardships of children who are disadvantaged by structural inequality—including structural racism—by accusing their parents and separating families." This is the system that healthcare providers are engaging when they call Child Protective Services (CPS; the agency name varies from state to state) in response to a parent's interest in feeding their child from their body. Yet numerous anecdotal reports from parents with HIV reveal providers threatening or actually making such calls when they expressed a desire to breast/chestfeed. Such threats may deter breast/chestfeeding through fear; they can also drive people to breast/chestfeed in secret, without clinical support.

The new guidelines update specifically warns against making such calls, pointing out that they "exacerbate the stigma and discrimination experienced among people with HIV; and are disproportionately applied to minoritized individuals, including Black, Indigenous, and other people of color."

Reports indicate that a CPS paper trail, even from unsubstantiated calls, can cause ongoing harm to families. Further, we know from years of advocacy and inquiry around HIV criminalization that legal punishment has no place in health promotion.

"While one may not always agree with the choices of the other," Covin said, "it is important that biases do not get in the way of engaging a parent in treatment and support that may be life changing."

There is more to learn—and improved chances to find out.

Findings from large studies in resource-limited regions is strong. Still, many years of formal prohibition against breastfeeding while living with HIV in high-resource regions have, predictably, hampered U.S.-based research in this arena. The current guidelines are "partly based in evidence, and partly in identifying what we don't know yet," stated expert panel member Judy Levison, MD, MPH, at a recent workshop.

Levison, an HIV-expert OB/GYN at Baylor College of Medicine whose clinic has done groundbreaking work around perinatal peer support and breast/chestfeeding with parents living with HIV, has presented frequently on the timeline of research and guidelines around breast/chestfeeding and HIV. She often ends these presentations with examples of unanswered questions, such as: What is the level and role of parents' HIV meds in breast milk? How long must a person have an undetectable viral load before breast/chestfeeding is considered "safe"? What is the role of preventive regimens for infants when the breastfeeding parent's viral load is undetectable? How often should breastfeeding parents' viral loads be measured? The list ends with an ask to listeners: *What do you want to know?* With the support of federal guidance, the field for exploration by researchers, providers and parents is now wider. PA

CALL the National Perinatal HIV Hotline to reach national perinatal HIV experts, 24 hours a day, seven days a week: 888-448-8765.

SCAN THIS QR CODE to access talking points and other resources from The Well Project that can support conversations with providers about infant-feeding options, or **GO TO** thewellproject.org/hiv-information/resources-talk-your-provider-about-breastfeeding-and-hiv.

OLIVIA G. FORD (she, her; they, them) is a freelance editor and writer, past perinatal health advocate and editorial director for The Well Project, an online information, support and advocacy resource serving women living with HIV across the gender spectrum. She has worked primarily in HIV-related media since 2007. Her work has appeared in Black AIDS Weekly, POSITIVELY AWARE, POZ, Rewire and TheBody/TheBodyPro, among other outlets.

POSITIVELY AWARE

For pagination purposes, this page has been intentionally left blank.

PHOTO:

POSITIVELY AWARE

For pagination purposes, this page has been intentionally left blank.

PHOTO:

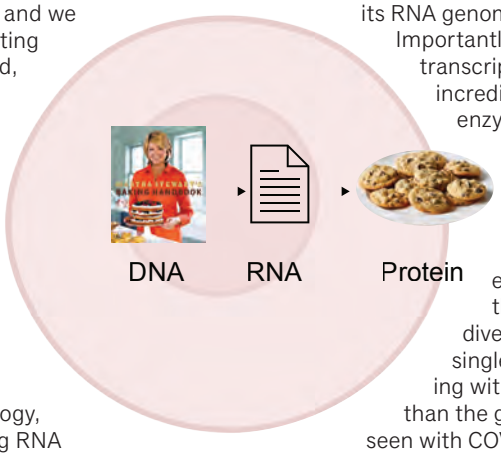
What makes HIV such a *retro*-virus?

Implications for treatment and cure

BY **JARED STERN, PHD**

Before diving into the complexities of HIV biology, it is important to understand the basic tenets of biology—how we use genetic information to produce fully-functional proteins, or what is known as the "central dogma" of biology. Deoxyribonucleic acid (DNA) is the genetic code in all cells' nuclei that encodes for everything our cells—and bodies—need to function. The DNA code is read by cells and messenger molecules called ribonucleic acid (RNA) are made. These messenger RNAs can leave the nucleus and be read by other machinery to produce proteins of various functions. In skin cells, this protein might be melanin for UV protection or for hair follicle cells, this protein might be keratin that forms the hair itself. For CD4+ T cells—the immune cell infected by HIV—these proteins may be the various chemokines and cytokines needed to fight off infection.

This process of reading DNA to make RNA and finally protein can be thought of much the same as reading a recipe book to cook a meal. DNA is the recipe book containing all of the recipes needed to make a meal, but we don't necessarily want to take this recipe book into the kitchen—it takes up far too much space on the counter and we don't want to risk getting the book dirty. Instead, a photocopy of the recipe is made and brought into the kitchen to read, just like how DNA is copied into RNA that is transported across the cell to make protein whilst the DNA cookbook stays put on the bookshelf (the cell's nucleus). In biology, the process of making RNA from DNA is called "transcription" as DNA and RNA are the same language as each other, whereas making protein from RNA is called "translation"—languages switch from RNA (or, words in a recipe book) to protein (the actual meal that is made). Every time a cell needs to make a protein, it will *transcribe* the recipe from its DNA into RNA which will then be *translated* into the protein it needs.



So, what about HIV? Unlike humans' DNA genome, HIV has an RNA-based genome. This means that after HIV binds to its receptors (CD4 and CCR5 or CXCR4) on the surface of a CD4+ T cell and releases its cargo into the cell, the virus needs to convert its RNA into DNA for the viral recipes to be in a language that the cell understands. To do this, the virus uses its reverse transcriptase enzyme to *reverse transcribe* the RNA into DNA. This step is said to go against the central dogma of biology and is why HIV is classified as a "retrovirus." Reverse transcriptase inhibitors act to block the virus from converting its RNA genome into DNA.

Importantly, reverse transcriptase is an incredibly error-prone enzyme, quickly creating mutations that can lead to drug resistance. In fact, HIV is such an error-prone virus that the genetic diversity seen in a single individual living with HIV is greater than the genetic diversity seen with COVID-19 globally.

Once HIV reverse transcribes its RNA genome into DNA, another unique aspect of HIV biology occurs: integration. HIV's integrase enzyme integrates its viral DNA into the infected cell's DNA so that it is permanently embedded in the cell's genome, analogous to someone sticking in their own recipe into our recipe book. From here, the cell does not recognize that there is anything wrong with its DNA; it sees a recipe, reads it and produces the meal that the recipe encodes for. Except, this time the cell is making new HIV virions rather than the proteins it needs for its function. This is much the same as when Rachel, from the TV show, *Friends*, one Thanksgiving wants to prove her skills in the kitchen by making a trifle but halfway through a recipe for trifle with cream and berries, the pages of her cooking magazine get stuck together. So, when Rachel goes to turn the page, she accidentally starts reading a recipe for shepherd's pie and ends up making a half-trifle, half-shepherd's pie Thanksgiving meal.

Importantly, all current licensed antiretroviral therapy (ART) drugs—except for the newly approved lenacapavir—act pre-integration. Fusion inhibitors, CCR5 antagonists and post-attachment inhibitors prevent a virus from binding to and fusing itself with a cell. Reverse transcriptase inhibitors prevent a virus from converting its RNA genome into DNA, and integrase inhibitors prevent HIV from integrating its DNA into the cell's. Protease inhibitors prevent another viral enzyme, protease, from maturing an HIV virion so it is unable to infect a new cell. Combinations of these drugs are incredibly effective at preventing cells from being infected except since they all act pre-integration, they cannot do anything for a cell that is already infected with HIV DNA integrated into its DNA. Once a cell is infected with HIV, it will remain infected as long as the cell survives and if the cell divides, so too does HIV. The cells that HIV infects, CD4+ T cells, are incredibly long-lived and divide a lot as part of our immune response; we want an immune cell to live for a long time in case we encounter a pathogen again and if we do encounter a pathogen, we want our immune cells to divide a lot to fight off the infection throughout our body. Unfortunately though, this is also why HIV is a lifelong infection and why ART alone does not cure HIV. How these infected cells are able to survive and divide for so long is the topic of much scientific research.

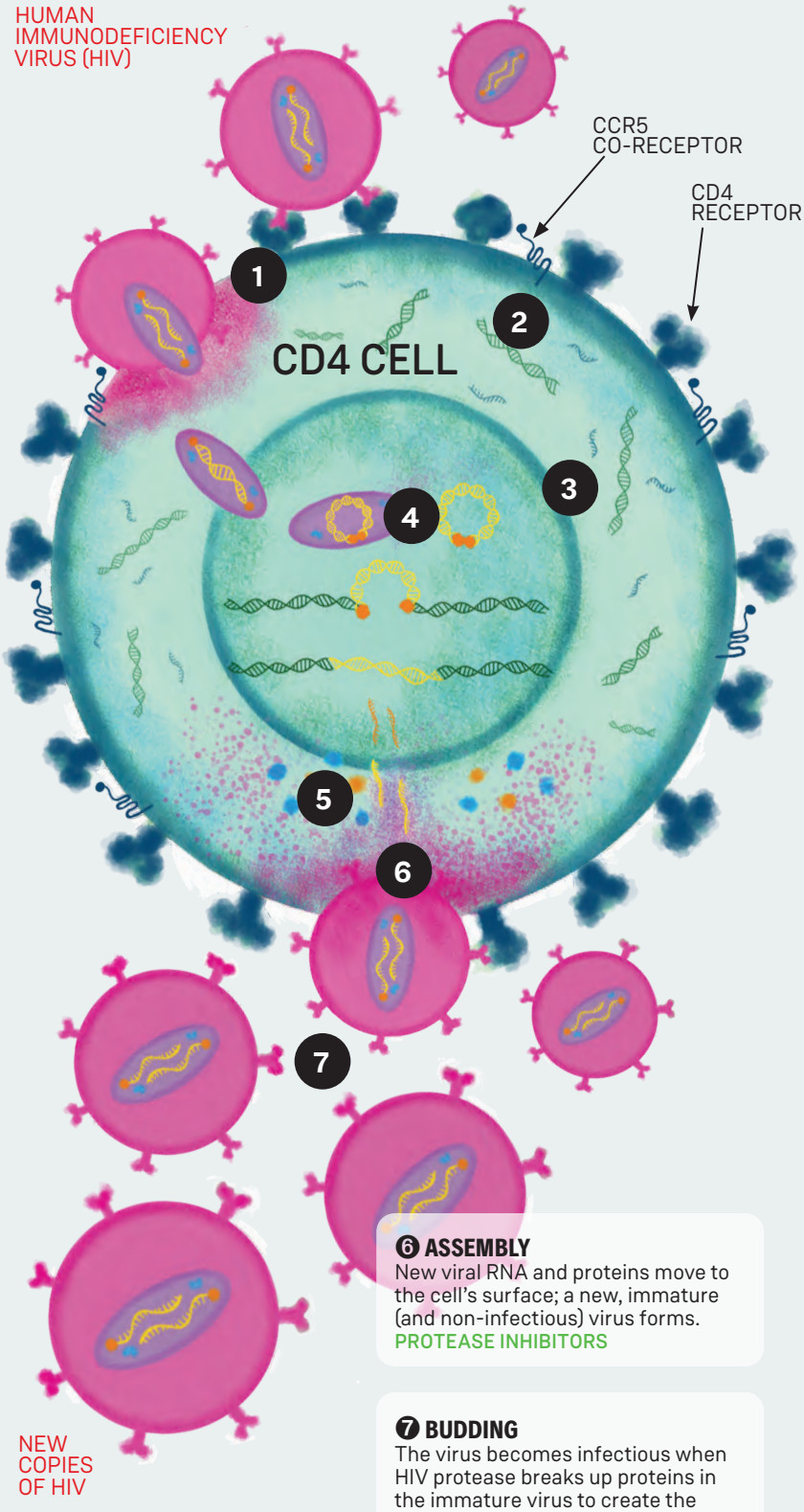
JARED STERN, PHD has been living with HIV since 2015 and has been involved in HIV advocacy and HIV research since 2016. They are currently a post-doctoral research fellow at the Fred Hutchinson Cancer Center, investigating the mechanisms of persistence of the latent HIV-1 reservoir in people living with HIV on suppressive antiretroviral therapy. Jared is passionate about basic science research, fostering strong relationships between HIV researchers and community, and improving the autonomy of people living with HIV through scientific literacy to combat stigma.

COURTESY OF JARED STERN

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

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 (DHHS).

The scientific evidence for HIV treatment is so strong that DHHS 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 31.

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 (**SEE** below).

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

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

Only three HIV medications qualify for use as rapid ART under DHHS and International AIDS Society-USA guidelines. They are:

1. Biktarvy
2. Tivicay + TAF or TDF + FTC or 3TC (basically, Tivicay plus Descovy or Truvada)
3. 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 DHHS) 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 DHHS 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

ISTOCK

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. 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 upfront 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.

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

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.") The *2023 Positively Aware HIV Drug Guide* used prices listed in Micromedex's Red Book guide.

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 70) 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. HIV treatment guidelines from DHHS
clinicalinfo.hiv.gov

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

HIV drug interactions calculator
hiv-druginteractions.org

Successful HIV treatment stops sexual transmission of the virus

Individuals on successful HIV therapy are unable to pass the virus on to their sex partners. This is called "treatment as prevention," or TasP. It means being on HIV antiretroviral treatment (ART) and undetectable with less than 200 copies for at least six months. It also goes by "undetectable equals untransmittable," or U=U.

PEP and PrEP: HIV prevention medications

PEP and PrEP are not HIV treatment, but are HIV medications used by HIV-negative people to prevent infection with the virus.

PEP stands for "post-exposure prophylaxis" and is taken for 28 days following a potential exposure to the virus; PEP must be started within 72 hours after a possible exposure.

PrEP stands for "pre-exposure prophylaxis" and is taken before a potential exposure to the virus.

Prophylaxis means "preventative."

Apretude is used as one injection given every two months. Descovy for PrEP and Truvada for PrEP are taken as one tablet daily. (They may also be used as four tablets a week or even just around the time of sex, depending upon the guidelines followed.) See those three pages in this drug guide.

DHHS Guidelines for people starting HIV therapy for the first time

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

A complete HIV treatment regimen consists of medications from two or more drug classes. Some of these medications are combined into one pill:

A **single-tablet regimen** (STR) is a complete treatment all by itself. STRs include Biktarvy, Triumeq, Dovato, Juluca, Symtuza and Delstrigo.

A **long-acting injectable** (LAI) regimen is available: Cabenuva.

A **fixed-dose combination** (FDC) uses two or more medications and needs to be taken with a medication from at least one other drug class. FDCs include Descovy, Truvada and Prezcobix.

The HIV drug classes are:
Integrase strand transfer inhibitors (integrase inhibitors): INSTIs
Nucleoside reverse transcriptase inhibitors (refered to as "nukes"): NRTIs
Protease inhibitors (must be taken boosted with a PKE drug; see below): PIs
Non-nucleoside reverse transcriptase inhibitors ("non-nukes"): NNRTIs
Long-acting **capsid assembly inhibitor**: CAI
Entry inhibitors/Attachment inhibitors: EIs/AIs

Long-acting injectables from different drug classes are now available. A **pharmacokinetic enhancer** (PKE) is not an HIV drug, but is used to boost the drug level of a protease inhibitor.

KEY TO ACRONYMS

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

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.

THE FOLLOWING ARE AVAILABLE AS CO-FORMULATED DRUGS

(NOT A COMPLETE LIST)

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

★ Recommended initial regimens for most people who are living with HIV and do not have a history of using Apretude (for PrEP)

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

INSTI + 2 NRTIs

Biktarvy
BIC / FTC / TAF
A1

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

INSTI + 1 NRTI

Dovato
DTG / 3TC
A1

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

Generic drugs are available for ABC (abacavir; **see** Ziagen page) and 3TC (lamivudine; **see** Epivir page).

INSTI + 2 NRTIs

Tivicay
DTG

WITH

Descovy
FTC / TAF

OR

Truvada
FTC / TDF

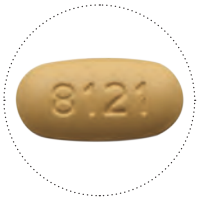
A1

A generic drug is available for Truvada (emtricitabine/tenofovir DF, FTC/TDF).

✔ Recommended initial regimen for people who are living with HIV and have a history of using Apretude (for PrEP)

INSTI genotypic resistance testing should be done before starting antiretroviral therapy (ART). If treatment is begun prior to results of genotypic testing, the following regimen is recommended (pending the results of the genotypic test):

Boosted darunavir + 2 NRTIs



Symtuza
DRV / COBI / FTC / TAF
A111

Prezcobix
DRV / COBI

OR

Prezista
DRV 800 mg

Norvir
RTV

WITH

Descovy
FTC / TAF

OR

Truvada
FTC / TDF

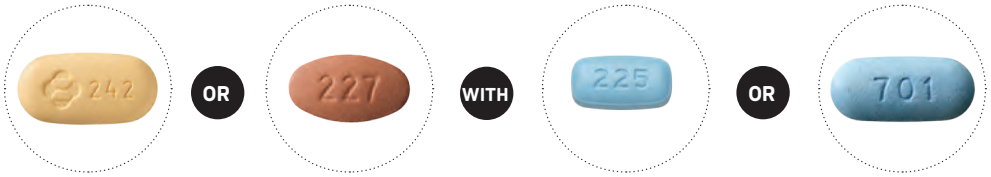
AIII

Generic drugs are available for Truvada (emtricitabine/tenofovir DF, FTC/TDF) and Norvir (ritonavir, RTV).

✔ Recommended initial regimens in certain clinical situations

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

INSTI + 2 NRTIs



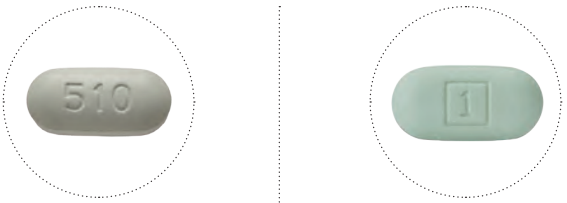
Isentress HD (2 tablets once daily) or **Isentress** (1 tablet twice daily)
RAL

Descovy
FTC / TAF
B2

Truvada
FTC / TDF
B1

A generic drug is available for Truvada (emtricitabine/tenofovir DF, FTC/TDF).

Boosted INSTI + 2 NRTIs

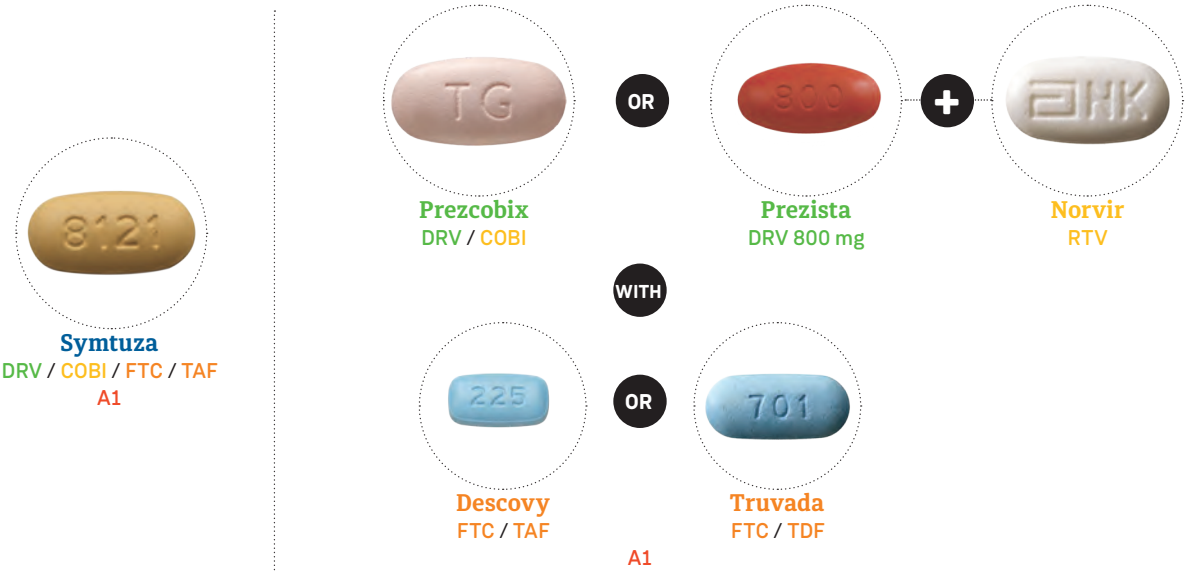


Genvoya
EVG / COBI / FTC / TAF
B1

Stribild
EVG / COBI / FTC / TDF
B1

Boosted PI + 2 NRTIs

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



Symtuza
DRV / COBI / FTC / TAF
A1

Prezcobix
DRV / COBI

Prezista
DRV 800 mg

Norvir
RTV

Descovy
FTC / TAF

Truvada
FTC / TDF

A1

Generic drugs are available for Truvada (emtricitabine/tenofovir DF, FTC/TDF) and Norvir (ritonavir, RTV).

✔ Recommended initial regimens in certain clinical situations (continued)

Boosted PI + 2 NRTIs

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

Evotaz
ATV / COBI

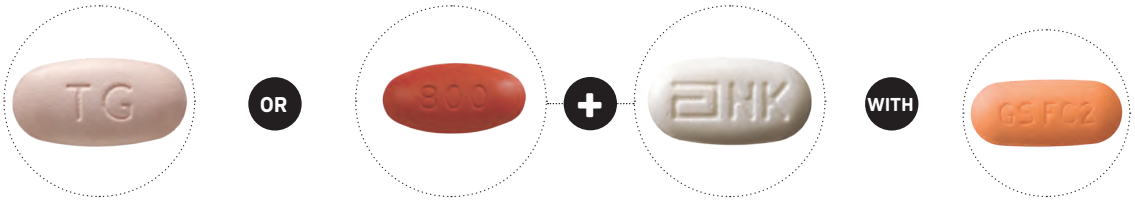
Reyataz
ATV

Norvir
RTV
B1

Descovy
FTC / TAF

Truvada
FTC / TDF

Generic drugs are available for Reyataz (atazanavir, ATZ), Norvir (ritonavir, RTV) and Truvada (emtricitabine/tenofovir DF, FTC/TDF).



Prezcobix
DRV/ COBI

Prezista
DRV 800 mg

Norvir
RTV
B2

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

Generic drugs are available for Norvir (ritonavir, RTV), ABC (abacavir; **see** Ziagen page) and 3TC (lamivudine; **see** Epivir page).

NNRTI + 2 NRTIs

Delstrigo
DOR / 3TC / TDF
B1

Pifeltro
DOR

Descovy
FTC / TAF

B3

Generic drugs are available for 3TC (lamivudine; **see** Epivir page) and TDF (tenofovir DF; **see** Viread page).

NNRTI + 2 NRTIs

3TC may substitute for FTC and vice versa

Atripla
EFV 600 mg / FTC / TDF
B1

Symfi
EFV 600 mg / 3TC / TDF
B1

Symfi Lo
EFV 400 mg / 3TC / TDF
B1

Sustiva
EFV 600 mg

Descovy
FTC / TAF

B2

Generic drugs are available for Atripla (**see** Symfi and Symfi Lo page), EFV (efavirenz; **see** Sustiva page), FTC (emtricitabine; **see** Emtriva page), TDF (tenofovir DF; **see** Viread page), 3TC (lamivudine; **see** Epivir page) and Sustiva (EFV, efavirenz).

✔ Recommended initial regimens in certain clinical situations (continued)

NNRTI + 2 NRTIs
3TC may substitute for FTC and vice versa

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

Odefsey
RPV / FTC / TAF
B2

Complera
RPV / FTC / TDF
B1

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

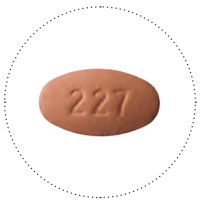
Except for individuals with pre-treatment HIV viral load greater than 500,000 copies/mL, who are known to have active hepatitis B virus (HBV) coinfection, or who will start ART before results of HIV genotype testing for reverse transcriptase or HBV testing are available

Dovato
DTG / 3TC
A1

Prezista
DRV 800 mg

Norvir
RTV

WITH



Isentress
(one tablet twice daily)
RAL

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

A generic drug is available for Norvir (ritonavir, RTV).

Prezista
DRV 800 mg

Norvir
RTV

WITH

Epivir
3TC

Generic drugs are available for Norvir (ritonavir, RTV) and Epivir (lamivudine, 3TC).

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

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

HIV PREVENTION

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

NON-HIV DRUGS

66	**Egrifta SV**	tesamorelin for injection	for HIV-related hard belly fat
66	**Mytesi**	crofelemer	for HIV/AIDS-associated diarrhea
67	**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

★ DHHS recommended initial regimen for most people

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 and no known resistance to components of the regimen.

For adults and children weighing at least 55 pounds (25 kg), use standard dose above or see package labeling. New pediatric formulation available for children at least 2 years old and weighing 30.8–55 pounds (14–25 kg), Biktarvy Low Dose, 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. DHHS guidelines recommend closely monitoring people with pre-existing psychiatric conditions. Prior to initiation, test for hepatitis B virus (HBV). Severe exacerbations of HBV have been reported in people with co-infection who have discontinued Biktarvy (due to elimination of the emtricitabine and TAF components, which also treat HBV). Monitor liver enzymes closely. Initiation of HBV therapy may be warranted upon discontinuation of Biktarvy. Call your health care provider right away if you develop any of the following signs of hepatitis: yellowing of the skin or whites of the eyes; dark or tea-colored urine; pale-colored bowel movements; nausea or vomiting; loss of appetite; or pain, aching, or tenderness on the right side below the ribs.

POTENTIAL DRUG INTERACTIONS

Do not take with rifampin or dofetilide. Not recommended to be taken with Cimduo or Temixys, Descovy, Emtriva, Epivir-HBV, Hepsera, Truvada, Vemlidy, or Viread, all for treatment of hepatitis B, as the emtricitabine and tenofovir components of Biktarvy already treat HBV. Biktarvy can be taken at least two hours before or six hours after taking laxatives or antacids, sucralfate, oral iron or calcium supplements (but either of these two can be used with Biktarvy if taken with food at the same time), or buffered medications. Start metformin at lowest dose and titrate based on tolerability and clinical effect. Monitor for metformin adverse effects. When starting or stopping Biktarvy in people on metformin, dose adjustment of metformin may be necessary to maintain optimal glycemic control. Not recommended with St. John's wort. Can be taken with Epclusa, Harvoni, Sovaldi, and Vosevi. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Biktarvy is widely prescribed because of its efficacy, safety, and drug resistance profile. 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 are accumulating that show Biktarvy works for people who have detectable virus when they switch to it from another regimen (having experienced virologic failure on their previous regimen). However, people who have previously experienced virologic failure when using another integrase inhibitor, such as Isentress or Tivicay, are more prone to losing virologic control after switching to Biktarvy. There aren't sufficient data to support the initiation of Biktarvy during pregnancy. People who become pregnant while on Biktarvy 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.

DR. MELANIE THOMPSON: With a few exceptions, Biktarvy is recommended for initial therapy for most people with HIV, including for "rapid" or "same-day" start of HIV treatment. Pregnant people, however, should not begin Biktarvy because safety and efficacy data are lacking in pregnancy. Those who become pregnant with suppressed virus on Biktarvy should discuss with their care providers whether continuing the drug with close monitoring is an option. An important new issue has arisen because of INSTI resistance that emerged during PrEP studies with long-acting cabotegravir (Apretude). Guidelines now recommend that people who have acquired HIV after exposure to cabotegravir should not begin an INSTI-based regimen unless an INSTI genotype is available, due to possible cabotegravir resistance and cross-resistance to other INSTIs. (See more under Apretude.) Studies suggest that people with suppressed virus on dolutegravir (Tivicay) + TDF/FTC, TDF/3TC, or TAF/FTC may safely switch to Biktarvy, even in the presence of a past M184V mutation.

There are few drug-drug interactions with Biktarvy, although some are important. Dofetilide, a medication for heart rhythm disturbances cannot be co-administered because serious heart rhythm disturbances could occur. Some medicines for seizures or tuberculosis and the herbal supplement 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, or iron can decrease Biktarvy levels and are a common source of blips or persistent low-level viremia. Biktarvy should be taken at least 2 hours before or 6 hours after these supplements if fasting, although calcium and iron can be taken simultaneously with Biktarvy if taken with food.

Weight gain can be associated with INSTIs, especially dolutegravir and bictegravir, and also with TAF. It's important to watch your diet and stay physically active regardless of what you are taking, but this is especially true with a TAF + INSTI combo. All INSTIs have the potential for insomnia or, rarely, worsening of depression or suicidal ideation, particularly if there are pre-existing mental health issues. Bictegravir elevates the blood creatinine level by just a small amount, about 0.1 mg/dL, but this is because of blocking creatinine secretion in the kidney, not because of kidney toxicity, and occurs within weeks of starting bictegravir.

ACTIVIST JOEY WYNN: Biktarvy is 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 prefer taking pills (as opposed to an injectable medication) and is ideal for people just starting their first regimen. Pricing can be a concern in some scenarios, but resources are available to help defray or remove costs based on your situation. Biktarvy definitely has the lion's share of the field for now.

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

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

STANDARD DOSE

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

Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. Dovato is not recommended for people who have severe liver impairment. According to the drug label, Dovato is not recommended for people with decreased kidney function (now down to a creatinine clearance less than 30 mL/min) due to the lamivudine component. This medication combination, however, is often used in reduced renal function below 30 mL/min because of the relatively minimal risk of lamivudine accumulation and side effects. In addition, reduced doses may be obtained by using the individual components of this medication as needed.

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

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Dolutegravir and lamivudine are both generally well tolerated. Side effects occurring in at least 2% of study participants receiving Dovato included headache, nausea, diarrhea, insomnia, fatigue, and dizziness. INSTIs are associated with weight gain. Dolutegravir can cause a small, reversible increase in kidney function test (serum creatinine) within the first few weeks of treatment that does not affect actual kidney function. There have been rare reports of depression and suicidal ideation with INSTIs, primarily in people with a history of psychiatric illnesses. DHHS guidelines recommend closely monitoring people with pre-existing psychiatric conditions. Prior to initiation, test for hepatitis B virus (HBV). Severe exacerbations of HBV have been reported in people with HBV co-infection who have discontinued Dovato (due to elimination of the lamivudine component, which also treats HBV). Monitor liver enzymes closely. Initiation of HBV therapy may be warranted upon Dovato discontinuation. Call your health care provider right away if you develop any of the following signs of hepatitis: yellowing of the skin or whites of the eyes; dark or tea-colored urine; pale-colored bowel movements; nausea or vomiting; loss of appetite; or pain, aching, or tenderness on the right side below the ribs.

POTENTIAL DRUG INTERACTIONS

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

MORE INFORMATION

Basically, this medicine is Triumeq without the abacavir component (brand name Ziagen, also found in Epzicom). Dolutegravir is from the powerhouse drug class of integrase inhibitors, which are highly effective and generally tolerable. The benefits of using a two-drug regimen for HIV include less exposure to HIV medication while maintaining viral suppression and minimizing the potential for side effects. At one, two, and nearly three years into the GEMINI-1 and GEMINI-2 studies, DTG + 3TC was found to be non-inferior to the triple drug regimen of DTG + Truvada (emtricitabine and tenofovir DF combined in one pill). At the 144-week point, for the two studies, 82% (584 out of 716 individuals) had undetectable viral load, compared to 84% (599 out of 717) of those taking the three-drug therapy. Everyone in the study was taking HIV treatment for the first time, and 20% of them had a high viral load of more than 100,000 copies per mL when entering the clinical trials. Dovato has also been successful for treatment-experienced people switching to it after being undetectable (viral load less than 50 copies per mL). The TANGO study evaluated treatment switch from TAF-containing regimens with three or more drugs to the two-drug regimen of dolutegravir/lamivudine and, at both 48 and 96 weeks, found Dovato to be non-inferior to the three-drug regimen standard of care. Weight gain is being increasingly recognized as a side effect of INSTIs. Although dolutegravir is now a preferred medication during pregnancy as well as for people who are trying to conceive, U.S. HIV perinatal treatment guidelines suggest using three-drug regimens. Find the discussion on page C-53 of perinatal guidelines at hivinfo.nih.gov. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

DR. MELANIE THOMPSON: The only two-drug regimen recommended for initial treatment, Dovato is great for many people, but shouldn't be taken if you have hepatitis B, virus that is resistant to 3TC/FTC, or a viral load above 500,000 copies/mL. Dovato isn't recommended for same-day treatment because a genotype, hepatitis B serology, and a viral load will not be available to guide choice of therapy. 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. Weight gain with dolutegravir remains a concern, as well as the other possible INSTI side effects (insomnia and new or worsening depression). 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.

The price of Dovato (monthly wholesale acquisition cost of $2,652) is over $641 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. For more information on dolutegravir, see Tivicay.

ACTIVIST JOEY WYNN: Some folks are looking to take fewer medications; a 2-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 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're wanting to reduce the medications you're taking.

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

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

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

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

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

POTENTIAL SIDE EFFECTS AND TOXICITY

The most common side effects include insomnia, headache, and fatigue. Data associate INSTIs with weight gain. The pediatric ODYSSEY/PENTA-29 trial reported in 2021 did not observe the weight gain seen in adults. DTG can cause a small, reversible increase in serum creatinine within the first few weeks of treatment, but does not affect actual kidney function. There have been rare reports of depression and suicidal ideation with INSTIs, primarily in people with a history of psychiatric illnesses. DHHS guidelines recommend closely monitoring people with pre-existing psychiatric conditions. Conflicting data suggest people who have a high risk of cardiovascular problems have a potential for heart problems when using abacavir-containing regimens. Monitor for signs of hypersensitivity reaction (HSR) to abacavir. Prior to starting Triumeq, all individuals should take 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 O.K. to use. Avoid co-administration with oxcarbazepine, phenobarbital, phenytoin, or St. John's wort. Start metformin at lowest dose and titrate based on tolerability and clinical effect. Monitor for metformin adverse effects. Avoid use of sorbitol-containing medicines with lamivudine; there are many, such as acetaminophen liquid (Tylenol liquid and others). May increase levels of dalfampridine, which may increase the risk of seizures. When taking carbamazepine, 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. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

DR. MELANIE THOMPSON: In 2022, the IAS-USA Antiretroviral Guidelines Panel removed Triumeq from the list of regimens recommended for initial HIV treatment due to longstanding concerns that abacavir increases the risk of cardiovascular disease, and to the risk of abacavir hypersensitivity—which can be a very serious side effect—requiring an HLA-B*5701 genetic test prior to prescribing. Now that there are other options, such as Dovato, the benefit of Triumeq appears to have waned. The federal HHS guidelines panel, however, retains Triumeq as an option, while cautioning to avoid abacavir in persons with or at high risk for cardiovascular disease. Both panels agree that Triumeq cannot be used for "rapid" or "same day" start of ART, before labs have returned.

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 can be 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, and talk with your HIV care provider if you are taking metformin or medications for seizures or tuberculosis. For more info on drug interactions, see the comments about Tivicay. Early concerns about an increased risk of birth defects (specifically neural tube defects) in infants exposed to dolutegravir at the time of conception have been largely put to rest by new data showing no significant difference in neural tube defects between persons on dolutegravir and those on non-dolutegravir-containing regimens. The very small and not statistically significant risk should be discussed with persons of childbearing potential who are starting Triumeq, and all pregnant people should take folate supplements to decrease the risk of neural tube birth defects. (See 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-to-drug interactions that make it a second line choice. Talk to your provider and figure out if this is the one for you. People with hepatitis B should definitely pass on this option.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$4,244.88/month

Juluca

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

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

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

STANDARD DOSE

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

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

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

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Both dolutegravir and rilpivirine are generally well tolerated. Side effects observed in greater than 2% of study participants were diarrhea and headache. Data associate INSTIs with weight gain. Dolutegravir and rilpivirine can each cause a small, reversible increase in a kidney function test (serum creatinine) within the first few weeks of treatment without affecting actual kidney function. There have been rare reports of depression and suicidal ideation with INSTIs, primarily in people with a history of psychiatric illnesses. DHHS guidelines recommend closely monitoring anyone with pre-existing psychiatric conditions. Liver enzymes should be monitored in people with hepatitis B or C and taking dolutegravir. Call your health care provider right away if you develop any of the following signs of hepatitis: yellowing of the skin or whites of the eyes; dark or tea-colored urine; pale-colored bowel movements; nausea or vomiting; loss of appetite; or pain, aching, or tenderness on the right side below the ribs.

POTENTIAL DRUG INTERACTIONS

Do not take Juluca with rifampin, rifapentine, or the anti-arrhythmic dofetilide (a heart medication). If taking rifabutin, add an Edurant tablet to Juluca dose. If you take antacids, laxatives, or other products that contain aluminum, calcium carbonate, magnesium, or buffered medicines, Juluca should be taken—with a meal, as always—at least 4 hours before or 6 hours after you take these medicines. Alternatively, these medications can be taken at the same time with Juluca and 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, oxcarbazepine, phenobarbital, and phenytoin) or St. John's wort. DHHS HIV treatment guidelines suggest that metformin be started at the lowest dose and titrated based on tolerability and clinical effect. Monitor for metformin adverse effects. When starting or stopping Juluca in people taking metformin, dose adjustment of metformin may be necessary to maintain optimal glycemic control. Not intended to be taken with other HIV medications, unless prescribed that way. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Juluca was the first two-drug combination approved as a complete regimen for HIV. It replaces a three- or four-drug therapy for people with undetectable viral loads who want to switch to a simpler or smaller tablet regimen. Juluca still works against two stages of the virus life cycle, as do the three-drug regimens. The guidelines cite Juluca as "a reasonable option when using nucleoside drugs is not desirable"—for example, due to previous toxicity—with an A1 rating (strong recommendation based on randomized controlled trials). Juluca is the smallest STR, which may be advantageous to individuals who have difficulty swallowing. For individuals with HIV-2, commonly found outside the U.S., an NNRTI would not be recommended, as HIV-2 is inherently resistant to NNRTIs. Rilpivirine is an alternative drug for use during pregnancy, and although dolutegravir is now a preferred medication in pregnancy as well as for people who are trying to conceive, U.S. HIV perinatal treatment guidelines suggest using three-drug regimens. Find the discussion on page C-53 of perinatal guidelines at hivinfo.nih.gov. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

DR. MELANIE THOMPSON:

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. Don't take Juluca if you have hepatitis B, as neither of the drugs in it has activity against that virus. There are a number of drug interactions with Juluca. Like all dolutegravir-containing regimens, it cannot be taken with dofetilide, some medications for seizures and tuberculosis, or St. John's wort. Dolutegravir increases metformin levels, so talk with your care provider if you are taking this drug. Dexamethasone and acid blockers should be avoided as they decrease levels of rilpivirine, dolutegravir, or both. Juluca should be taken 4 hours before or 6 hours after taking sucralfate or products containing aluminum, magnesium, calcium, or iron on an empty stomach. Calcium and iron can be taken together with Juluca only if taken with a meal. 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 kidney secretion of creatinine rather than kidney toxicity. (For further information about dolutegravir and rilpivirine, see Tivicay and Edurant.)

Early concerns about an increased risk of birth defects (specifically neural tube defects) in infants exposed to dolutegravir at the time of conception have been largely put to rest by new data showing no significant difference in neural tube defects between persons on dolutegravir and those on non-dolutegravir-containing regimens. The very small and not statistically significant risk should be discussed with persons of childbearing potential who are starting Juluca, and all pregnant people should take folate supplements to decrease the risk of neural tube birth defects. (See Tivicay.)

Because of similarities between cabotegravir and dolutegravir, some have suggested that Juluca might be used as a bridging drug if doses of Cabenuva have to be missed. This seems reasonable but has not been studied in clinical trials. Oral cabotegravir and rilpivirine are supplied by ViiV at no cost for persons on Cabenuva. For more information about Juluca, see comments on Tivicay and Edurant.

ACTIVIST JOEY WYNN:

Juluca was the first two-drug pill; six years later, I believe the benefits do not outweigh the difficulties of this option. Many drug-to-drug interactions and numerous reports of diarrhea and headaches make this a difficult choice in this era. The timing of taking this with other items such as vitamins and other OTC products make this a complicated lifestyle to manage. I do not know of anyone still on this from before 2021. I'm sure for a handful of folks this works and they don't want to switch, but for those about to select a new therapy, this might not be a good option.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$3,978.37/month

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, DHHS 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 women in their first trimester continue taking efavirenz as long as their viral load remains undetectable; however, efavirenz should only be used if the potential benefit outweighs the potential risk (as when other treatment options are not available). 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 may need to be adjusted. Titrate 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.

ACTIVIST JOEY WYNN:

The gold standard for many years, Atripla fell out of favor due to CNS side effects 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. Every dog has its day, and this one is doggone. Symfi and Symfi Lo are "branded generic" versions of Atripla. Same issues apply, although the greatly reduced cost makes this have 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, DHHS 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 a new DHHS statement last year, "In a cross-trial analysis, DOR was not associated with weight gain compared with [efavirenz] 600 mg or boosted [darunavir]." TDF is still an effective and quite tolerable medication, but TAF has potentially less long-term renal and bone toxicity. Doravirine has not been directly compared to integrase inhibitor-based regimens in clinical trials yet. In the DRIVE-FORWARD study comparing doravirine to darunavir, at 96 weeks, 72% of treatment-naïve individuals in the doravirine group attained undetectable status (a viral load of less than 50 copies/mL), compared to 65% for the darunavir group. For individuals with HIV-2, commonly found outside the U.S., an NNRTI would not be recommended as HIV-2 is inherently resistant to NNRTIs. There are no data on the safe use of Delstrigo during pregnancy. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

DR. MELANIE THOMPSON: Delstrigo is the first STR to be coformulated with a newly approved drug and two generic drugs. Because none of the doravirine trials compared the drug to INSTIs, doravirine-containing regimens aren't recommended as initial therapy for most people in the U.S., although the Europeans have elevated Delstrigo to first line in the EACS guidelines. 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, or 3.74 lbs.) was more than with efavirenz (0.6 kg) and similar to that with ritonavir-boosted darunavir (1.4 kg) at 48 weeks, but all were similar at week 96. Delstrigo is not recommended in pregnancy due to insufficient data with 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 hope that doravirine might be genetically more robust and less likely to select for drug resistance, however, has been somewhat disappointing. With two generic drugs, you would expect Delstrigo's average wholesale cost to be lower than it is at $2,431 per month.

ACTIVIST JOEY WYNN: One of the first viable older formulations in a generic type of new formulation. Pricing is great, but an older regimen with a few negatives makes this a second-line option.

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

✔ Other complete HIV regimens, DHHS recommended initial therapy in certain clinical situations

STANDARD DOSE (FOR BOTH GENVOYA AND STRIBILD)

One tablet, once daily with food. For people taking HIV treatment for the first time (treatment-naïve) or individuals with suppressed viral load on a stable HIV regimen for at least 6 months who have no known resistance to the elvitegravir, emtricitabine, or tenofovir components of the regimen.

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. DHHS guidelines recommend closely monitoring people on an INSTI who have pre-existing psychiatric conditions. Prior to initiation, people should be tested for hepatitis B virus (HBV) infection. Severe exacerbations of HBV have been reported in people co-infected with HBV who have discontinued Genvoya or Stribild (due to elimination of the emtricitabine and tenofovir components, which also treat hepatitis B). Monitor liver enzymes closely in co-infection. HBV therapy may be warranted upon discontinuation. Call your health care provider right away if you develop any of the following signs of hepatitis: yellowing of the skin or whites of the eyes; dark or tea-colored urine; pale-colored bowel movements; nausea or vomiting; loss of appetite; or pain, aching, or tenderness on the right side below the ribs.

Before taking Genvoya or Stribild, kidney function testing should be conducted, including serum creatinine (SCr), serum phosphorus, urine glucose, and urine protein. These measurements should continue to be monitored while taking Genvoya or Stribild.

POTENTIAL DRUG INTERACTIONS

Do not take with Cimduo or Temixys, Descovy, Emtriva, Epivir-HBV, Hepsera, Truvada, Vemlidy, or Viread. Separate by at least 2 hours from antacids containing aluminum, magnesium hydroxide, or calcium carbonate. Safe to take with other medications used for heartburn and GERD such as Aciphex, Dexilant, Nexium, Pepcid, Prevacid, Prilosec, and Zantac. Cobicistat has many drug interactions similar to Norvir. Do not take with lovastatin or simvastatin, alfuzosin, carbamazepine, phenobarbital, phenytoin, ergotamine, dihydroergotamine, methyl-ergonovine, oral midazolam, lurasidone, pimozide, Revatio, rifampin, rifabutin, rifapentine, Serevent, triazolam, St. John's wort, clopidogrel, or ticagrelor. Rosuvastatin and atorvastatin should be used with caution and started at the lowest dose possible. Monitor closely for increased side effects, such as muscle pain, from these medications. An alternative corticosteroid to systemic dexamethasone should be considered. Risks versus benefits of using with voriconazole should be assessed with expert consultation. Concentrations of antidepressants such as fluoxetine, paroxetine, bupropion, or amitriptyline may be increased, and their doses may need to be reduced. Levels of many nasal and inhaled steroids like fluticasone may be increased, which may lead to symptoms of Cushing's syndrome. An alternative corticosteroid is recommended. Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours. Monitor for increased side effects of these medications. Effectiveness of oral contraceptives may be decreased; consider using alternative or additional contraception methods. Start metformin at lowest dose and titrate based on tolerability and clinical effect. Reduce Daklinza dose to 30 mg. Taking with Olysio, Viekira Pak, or Zepatier is not recommended. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are many other drug interactions not listed here.

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

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

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

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

ACTIVIST 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 their market domination. Although a shrewd strategy, it may have worked for a few 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.

MORE INFORMATION

Genvoya and Stribild are not recommended during pregnancy. Switching regimens should be considered for anyone who is pregnant, especially during the third trimester. 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

✔ Other complete HIV regimens, DHHS recommended initial therapy in certain clinical situations

STANDARD DOSE (FOR BOTH ODEFSEY AND COMPLERA)

One tablet once daily, with a standard meal. For people taking HIV therapy for the first time (treatment-naïve) or people with suppressed viral load on a stable HIV regimen for at least six months who have no known resistance to the components of the regimen: rilpivirine, emtricitabine, or tenofovir.

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

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

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

ACTIVIST JOEY WYNN: Although lighter on the side effects, this combo still has lots of drug-drug interactions based on people's feedback to me. Having to time it based on food intake makes this a less than stellar option for you in 2023. Hard pass based on 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. 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

✔ DHHS recommended as a component of initial regimen in certain clinical situations; also DHHS recommended for rapid ART for people with a history of using Apretude (for PrEP)

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.

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

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

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Darunavir contains a sulfa component, so use with caution in people with sulfa allergies. Side effects most commonly reported in studies include diarrhea (9%), rash (8%), nausea (6%), fatigue (4%), headache (3%), abdominal discomfort (2%), and flatulence (2%). While very rare (in less than 0.4% of those taking it), severe rash, accompanied in some cases by fever and/or elevations of AST/ALT (liver enzymes), can be life-threatening. Seek medical attention immediately. Data associate TAF with weight gain. Observational cohort studies reported an association between some PIs (including darunavir taken with ritonavir) and an increased risk of cardiovascular (CV) events. Data on darunavir + 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. Initiation or dose adjustments of insulin or oral hypoglycemic medications may be required for some individuals. Cannot be taken with Zepatier. Based on the mechanism of action, drug interactions with other hepatitis C medications are probably similar to the interactions with Prezcobix + Descovy. Not intended to be taken with other HIV medications, unless prescribed that way. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions that are not listed here.

MORE INFORMATION

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

DR. MELANIE THOMPSON: Symtuza, a 4-drug protease inhibitor-based STR, is 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 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.

For most people, the multitude of drug-drug interactions with COBI make unboosted 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. At $4,292 per month, 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 options. This is mainly due to the booster, which increases almost every medication in the bloodstream; not a good look in 2023.

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

✔ Complete HIV regimen DHHS recommended for people with viral suppression

STANDARD DOSE

Two long-acting intramuscular gluteal (butt muscle) injections once every two months. May be taken once monthly. Cabenuva consists of one injection of long-acting cabotegravir and one injection of long-acting rilpivirine. No food restrictions.

For adults 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). Oral rilpivirine must be taken with a meal. Initiate injections on the last day of oral lead-in or of your previous regimen. Initiation dose is 600 mg CAB LA + 900 mg RPV LA (3 mL each). Then for every other month dosing, continue with this dose for month 2, and then every other month thereafter. For monthly dose, continue with a lower maintenance dose of 400 mg CAB LA + 600 mg RPV LA (2 mL each) every month. Smaller dose may cause less pain or discomfort. See package insert for instructions on using the oral medications during planned or unplanned missed injections; oral medication should be taken until injections can be restarted. People may take Cabenuva up to 7 days before or after the date scheduled for injections. See package insert for instructions on missed doses. Increased monitoring is recommended when CrCl is less than 30 mL/min. The effect of severe liver impairment on Cabenuva is unknown. Longer needles (not included in the dosing kit) may be required for people with a BMI (body mass index) greater than 30.

➤ **SEE EDURANT;** oral cabotegravir is not commercially 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. The most common adverse reactions observed in 2% or more of people receiving Cabenuva in clinical trials were injection site reactions (83%, with 37% having at least Grade 2—moderate), 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 afterwards 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 (hepatotoxicity) 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. DHHS 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.

POTENTIAL DRUG INTERACTIONS

Cabenuva cannot be taken with carbamazepine, 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 (body mass index) greater than 30 kg/m^2. People with a history of exposure to an NNRTI may consider obtaining a GenoSure Archive resistance test to assess archived mutations that may decrease the susceptibility to rilpivirine. Pregnant 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: [For Dr. Thompson's complete comments, GO TO positivelyaware.com/cabenuva.] Cabenuva, the only complete HIV regimen that is injectable, is not approved for initial therapy or for individuals whose viral load is not suppressed, although studies are being conducted to look at its safety and effectiveness in this setting. Balancing out the convenience of dosing every two months is the slightly higher incidence of drug resistance seen in clinical trials of 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 is probably more frequently than you now go for HIV monitoring for your oral regimen. At present, injections cannot be self-administered. A common issue with Cabenuva is simply getting it covered by insurance. The cost is very high. It does not include administration charges or office visits. Reimbursement is confusing, and may depend on whether the drug is handled as a pharmacy benefit ... or as a medical benefit .... ViiV has a patient assistance program, but many patients and clinicians continue to struggle with access. Insurance denial has been a real obstacle for many patients who might benefit from this regimen, and the burden of arguing with insurance companies is a huge downside for clinicians who are simply trying to provide access to it.

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. Injections allow us to get on with our lives and not be weighed down with the daily burden of taking pills. 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.
If you want it, demand it—it's your choice. Some studies suggest the vast majority of those who got on an injectable will never go back to taking pills. I could go on about provider bias, but you get the point: get what you need to make your life work for you!

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

▼ Medication with unique mechanism of action, DHHS recommended for heavily treatment-experienced people

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.

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 an initiation dosing followed by the maintenance dose six months later.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

In the CAPELLA study, 65% of study participants experienced injection site reactions (ISRs) at Week 52 attributed to LEN. Most (44%) were mild (Grade 1) and resolved within 15 days. There was one discontinuation due to ISR. Nodules (bumps) and indurations (skin thickening) may be persistent. For Grade 3 and 4 laboratory abnormalities, 5% experienced hyperglycemia (high blood sugar), 6% experienced glycosuria (excess sugar in urine) and 13% experienced low creatinine clearance (eGFR) or high creatinine. The hyperglycemia, glycosuria, and creatinine changes observed were related to the individual's diabetes or were either transient or unconfirmed. Nausea occurred in 4% of participants given LEN.

POTENTIAL DRUG INTERACTIONS

Do not take with Evotaz or Reyataz (but can be taken with Prezcobix); the antimycobacterials carbamazepine, oxcarbazepine, phenobarbital or phenytoin; rifampin (taking with rifabutin or rifapentine is not recommended); or St. John's wort. Start the following medications at the lowest dose, titrate carefully and monitor for safety: dexamethasone, 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. 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 caution with triazolam and oral midazolam (Versed). O.K. 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). 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. The approval is for heavily treatment-experienced (HTE) individuals with resistance to multiple HIV drug classes in combination with other antiretrovirals. 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. Future drug development plans include lenacapavir-containing complete regimens, including a once-weekly pill, and use as a single drug for HIV prevention (PrEP). 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.

DR. MELANIE THOMPSON: [For Dr. Thompson's complete comments, GO TO positivelyaware.com/sunlenca.] Lenacapavir (LEN) is a first-in-class capsid inhibitor now FDA approved (in combination with other HIV therapy) for treatment of multidrug-resistant HIV in individuals whose virus is not responding to their current regimen. Approval was based largely on the 36 patients in cohort 1 of the CAPELLA study in people with multidrug-resistant virus.

At 26 weeks, 81% of the entire group had viral load below 50 copies/mL and an average gain of 75 CD4 cells/μL. Although the group was small, this was a good response for people with limited treatment options. There were no serious adverse events in either group, and the most common side effects were gastrointestinal symptoms and injection site reactions that were generally mild/moderate but tolerable.

Of concern, however, is that LEN resistance arose in 8 patients. This stresses the importance of having a strong backbone of active drugs to support LEN, which appears to have some genetic fragility. Excellent adherence with oral regimens and LEN will also be essential.

The FDA specifies two ways of dosing with LEN. The first requires oral LEN on the day of injectable dosing and the day after, or on days 1, 2 and 8 before injectable dosing starts on day 15. This allows levels of the drug to build quickly to decrease the possibility of resistance.

LEN also is subject to a fair number of drug-drug interactions that can be present up to nine months after the last dose. There are no interactions with gender affirming hormones or oral contraceptives.

And now, the price. Gilead says the 2 injections plus 2 or 3 lead-in pills of LEN will cost $42,250 for the first year of treatment, dropping to $39,000 for 2 injections annually (at $19,500 each.) That's an average of $3,250 a month for maintenance therapy in year two and beyond. But you won't be buying a month of drug at a time, so that nearly $20k expenditure could rack up a whopping co-insurance cost for a single dose. And what will happen for those on Medicare for whom company co-pay assistance programs do not work? Will endless rounds of "prior authorization" delay dosing and promote resistant virus? At the time of publication, it's too soon to tell. Let's just hope that Gilead makes this valuable drug available to people who need it without undue cost sharing.

ACTIVIST JOEY WYNN: Lenacapavir is the first in class of ARV drugs called capsid inhibitors. This treatment is specifically aimed at heavily treatment-experienced populations and long-term survivors. Since it was only FDA approved in December 2022, the jury is still out. This is another injectable in the long march towards a world of injectables, sub-dermals and other long-acting agents on the horizon. The future is definitely brighter with this new choice available.

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

▼ Medication with unique mechanism of action, DHHS recommended for heavily treatment-experienced people

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

At the time of approval in 2020, the most common side effect was nausea in 10% of study participants. Other side effects, observed less often, were diarrhea, 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.

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

MORE INFORMATION

Rukobia is 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. This causes the virus to accumulate in extracellular space and is subsequently removed by the body's immune system. 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.

DR. MELANIE THOMPSON: Fostemsavir is a first-in-class oral attachment inhibitor that prevents HIV from entering the T-cell. It is active against HIV that is resistant to all other classes and 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, and 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 safety 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.

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.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$10,205.72/month

Selzentry

maraviroc
MVC (EI)

EI **Entry inhibitor:** CCR5 antagonist

▼ Medication with unique mechanism of action, DHHS recommended for heavily treatment-experienced people

STANDARD DOSE

The recommended dose varies depending on other medications being taken but will be either 150, 300, or 600 mg twice daily (available in 150 mg and 300 mg tablets). Can be taken 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 as well as 25 mg, 75 mg tablets. Selzentry for children is dosed based on body weight. See the package insert or DHHS guidelines for weight-based dosing. The oral solution should be administered using the included press-in bottle adapter and oral dosing syringe.

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

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

POTENTIAL SIDE EFFECTS AND TOXICITY

The most common side effects occurring in greater than 8% of studied people include cough, pyrexia (fever), upper respiratory tract infections, rash, musculoskeletal symptoms, abdominal pain, and dizziness. Other less common side effects may include allergic reactions, liver toxicity, and heart problems in people with a history of heart disease. Rarely, Selzentry can cause dizziness or fainting when standing up due to low blood pressure. Caution should be used when administering Selzentry in people with a history of or risk factors for postural hypotension, cardiovascular comorbidities, or taking concomitant medication known to lower blood pressure. Stop taking Selzentry and contact your provider right away if you develop a rash, yellowing of your eyes or skin, dark urine, vomiting, or upper stomach pain. Selzentry should not be used by people with severe or end-stage kidney disease who are taking medications that can affect the level of Selzentry (check with your provider). Selzentry affects immune system cells and could possibly increase the risk of infections and cancer, although this has not been observed in studies with up to five years of follow-up, and some data indicate it may be beneficial in cancer or for preventing metastasis (the spread of cancer to other parts of the body).

POTENTIAL DRUG INTERACTIONS

Dose adjustments with other medications and anti-HIV drugs include: 150 mg twice daily if taken with medications that increase levels of Selzentry, such as boosted protease inhibitors, Stribild, Genvoya, Tybost, clarithromycin, and itraconazole; 300 mg twice daily if taken with Viramune, Isentress, Tivicay, Triumeq, Fuzeon, and all of the NRTIs and medications that do not affect the levels of Selzentry; and 600 mg twice daily if taken with medications that decrease levels of Selzentry, such as Atripla, Sustiva, Intelence, rifampin, and some anticonvulsants such as carbamazepine (Tegretol), phenobarbital, and phenytoin (Dilantin). Likely dose with rifapentine is 600 mg twice daily, but use with caution. Not recommended with St. John's wort. Selzentry may be co-administered with the hepatitis C medication Harvoni at a dose of 300 mg twice daily; however, ledipasvir (in Harvoni) may have potential to increase Selzentry levels. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

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

Selzentry is generally recommended only when HIV medications from other classes cannot be used or when a new class of medication is needed to construct a complete and durable treatment regimen for people who have drug resistance. Complex dosing, the need for a tropism test, and competition from newer drugs have dimmed some of the initial enthusiasm for this drug. In research bringing Trogarzo to market, Selzentry was often chosen to help create an optimized background regimen. Research participants had extensive HIV drug resistance. A tropism assay (Trofile, Trofile DNA, or HIV-1 Coreceptor Tropism with Reflex to UDS) is needed to determine if this medication will work. Results of a phenotypic tropism test (Trofile or Trofile DNA) may take up to a month to complete. Genotypic tests are also available and may provide a faster and less expensive alternative. Learn about Selzentry's mechanism of action at youtube.com/watch?v=oneYI0fhGa0. Selzentry only works for people with CCR5-tropic virus. Viral tropism refers to the types of HIV that a person can have, CCR5 (R5), CXCR4 (X4), or Dual-Mix Tropic (R5 and X4). Selzentry blocks CCR5, a co-receptor on the outside of a CD4 cell, and shuts down this point of entry for the virus. Most people have acquired R5 virus initially, and then over time, X4 and mixed viruses may predominate. Blocking R5 with Selzentry does not cause a shift to X4 or negatively affect disease progression or CD4 count in people whose virus can use dual-mix. The tropism test needed is now generally paid for by public health departments, Medicare, and private insurance. ViiV may cover the payment for the Trofile test under certain circumstances.

Selzentry seems to have minimal impact on lipid levels. DHHS guidelines do not recommend the use of maraviroc for treatment-naïve individuals who are pregnant. Anyone who becomes pregnant while taking maraviroc may continue if viral suppression is effective and the regimen is well tolerated. The pharmacokinetics of maraviroc are not significantly altered during pregnancy and no dosage adjustment is necessary. Maraviroc is known to have a moderate level of transfer across the human placenta, although insufficient data exist to evaluate the effects on a fetus. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

DR. MELANIE THOMPSON: The only approved CCR5 entry inhibitor, maraviroc is not for initial therapy. It may be helpful, however, for people who have substantial viral resistance and 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 will be discontinued as of January 1, 2024.

The monthly wholesale acquisition cost of Selzentry 300 mg is $1,633.

ACTIVIST JOEY WYNN: Selzentry, or maraviroc, is a CCR5 antagonist. Selzentry is for use only 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 those who are highly treatment-experienced and have limited treatment options.

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

Trogarzo

800 mg ibalizumab-uiyk
IBA (long-acting EI)

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

▼ Medication with unique mechanism of action, DHHS recommended for heavily treatment-experienced people

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 taken every two weeks thereafter. The maintenance dose can be administered as a diluted IV infusion or undiluted IV push. Must be taken in combination with another antiretroviral(s).

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

Trogarzo must be taken 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

Essentially, this drug is for heavily treatment-experienced people with multidrug resistance, along with an optimized background regimen (OBR). GO TO bit.ly/Trogarzo-mechanism-of-action to watch a YouTube video of its mechanism of action. A key point is that people must still take other HIV medications that have some activity—there has to be at least one HIV drug to which their virus is sensitive included in their OBR. DHHS HIV treatment guidelines list Trogarzo this way: "People with ongoing detectable viremia [detectable viral load] who lack sufficient treatment options to construct a fully suppressive regimen [get to undetectable viral load] may be candidates for the recently approved [in 2018] CD4 post-attachment inhibitor ibalizumab." Trogarzo is a newer option, but it does come with some rules. Non-adherence won't be an option—people won't be able to just show up whenever they want or be late to appointments when going to an infusion center. People must be on time. It is expensive because the cost of the drug is in addition to other expenses such as the time at the infusion center and cost for qualified individuals to administer and handle the medication, although there may be an option for people to receive their infusion at home. Infusions can also be done at clinics and at IV centers.

Although taken once every two weeks, because it must be used with other HIV medications, antiviral treatment will still be required to be taken daily. Other long-acting HIV drugs are on the way, however, and may be studied in combination with Trogarzo as well. Trogarzo is also the first HIV orphan drug—one that is produced for a relatively small population of people, fewer than 200,000. It was produced for people with multidrug-resistant HIV, estimated to be fewer than 40,000 in the U.S.; the company estimates there are fewer than 25,000. These are heavily treatment-experienced people who have multidrug resistance, and have, therefore, limited treatment options. Trogarzo has been shown to work against highly drug-resistant virus, when combined with an OBR. Data presented at ID Week 2020 showed evidence for long-term safety and efficacy as well as tolerability in people receiving Trogarzo for almost a decade. Trogarzo has also demonstrated CD4 improvements in clinical studies.

As a biologic, Trogarzo is the first HIV medication produced in cells rather than from chemicals. This does not make Trogarzo better, just different. Trogarzo works differently from any other HIV drug currently on the market. It binds to a domain (location) of the CD4 receptor (in this case, domain 2), blocking viral entry into the CD4 cell. Most HIV drugs target parts of HIV, which are variable and thus susceptible to resistance. Trogarzo works against both CCR5 and CXCR4 virus, and may be synergistic with some other classes of antiretrovirals. Resistance test results revealed no evidence of cross-resistance between Trogarzo and any of the approved classes of HIV drugs. Trogarzo is neither metabolized in the liver nor eliminated by the kidneys. Monoclonal antibodies such as ibalizumab are transported across the placenta as pregnancy progresses; therefore, the developing fetus has the potential to be exposed to Trogarzo. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

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

DR. MELANIE THOMPSON: Ibalizumab is an entry inhibitor (actually, a "post-attachment" inhibitor) with activity against multidrug-resistant HIV. It is only used for people who cannot otherwise construct a viable regimen. It requires intravenous infusions every 2 weeks. At a wholesale acquisition cost of $10,704 per month, 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. Lenacapavir [Sunlenca] may provide a new option for some people who are struggling with a viable regimen and who currently have no other option but to take Trogarzo.

ACTIVIST JOEY WYNN: Ibalizumab is the first drug in a new class called a CD4-directed post-attachment inhibitor. Trogarzo blocks the virus from entering CD4 cells. Trogarzo is for use only in highly treatment-experienced people, meaning 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 to 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**

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

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 seen in adults. There have been rare reports of depression and suicidal ideation, primarily among people with a history of psychiatric illnesses, in people receiving INSTI-based regimens. DHHS guidelines recommend closely monitoring people on an INSTI who have pre-existing psychiatric conditions. Tivicay can cause a small, reversible increase in kidney function test (serum creatinine) within the first few weeks of treatment without affecting actual kidney function. Liver enzymes should be monitored in people with hepatitis B or C.

POTENTIAL DRUG INTERACTIONS

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

MORE INFORMATION

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

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

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 recommended for all pregnant persons.

Weight gain has been associated with dolutegravir in some studies, particularly in women and African Americans. Weight gain appears to be higher when DTG is taken with TAF. Most weight gain occurs in the first year of therapy, so 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 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.

The average wholesale cost for Tivicay is $2,011 per month.

ACTIVIST JOEY WYNN:

Tivicay is safe, effective, and tolerable. This is a potent, relatively easy to take and "little to no" side effects from anyone I know taking this. In my region, the "Dolly Dezzy" combo (Dolutegravir/Descovy) is a great choice if you're O.K. with pills. On the down side, for some people, weight gain is a thing, for real.

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 DHHS recommended as a component of initial regimen in certain clinical situations

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 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. 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 DHHS guidelines recommend closely monitoring people with preexisting 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 O.K. to use. Raltegravir is not recommended with carbamazepine or phenobarbital. Raltegravir can be used with Harvoni, Zepatier, or Epclusa. Unlike Isentress, Isentress HD cannot be used with Intelence or boosted Aptivus. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions not listed here.

MORE INFORMATION

Isentress HD was approved in 2017. While the original formulation, Isentress, was well tolerated and highly effective, its twice-daily dose was seen by some as a relative inconvenience. According to DHHS HIV treatment guidelines, raltegravir was downgraded from a preferred component of an initial regimen in most individuals to a component of a regimen in only certain clinical situations due to the higher pill burden as well as the relatively lower genetic barrier against the development of resistance compared to second generation INSTIs. Raltegravir-based regimens may be preferred for people with high cardiovascular risk. Raltegravir is a preferred drug for PEP (post-exposure prophylaxis—preventing HIV acquisition after a potential exposure) along with dolutegravir. Isentress is one of the preferred INSTI medications in HIV treatment guidelines for pregnancy, 400 mg twice a day in combination with 2 NRTIs. In pediatric HIV guidelines, Isentress was downgraded in 2017 from "preferred" to an "alternative" part of an initial regimen for children ages 6–12, 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.
isentresshd.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 (other than in pregnancy) by DHHS or IAS-USA guidelines panels because newer INSTIs are less susceptible to viral resistance and can be taken once daily 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 taken at 400 mg twice daily. When taken with rifampin for tuberculosis, the dose of raltegravir is 800 mg twice daily.

ACTIVIST JOEY WYNN: About 16 years ago Isentress came onto the scene as the first 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 use of this older but easy to take treatment.

Prezista

darunavir
DRV

Prezcobix

800 mg darunavir, 150 mg cobicistat
DRV (PI), COBI (PKE)

PI — Protease inhibitor

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

✔ DHHS recommended as a component of initial regimen in certain clinical situations; also DHHS recommended for rapid ART for people with a history of using Apretude (for PrEP)

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 contains a sulfa component and should be used with caution by people with known sulfonamide allergy. Most common side effects may include diarrhea, nausea, headache, rash, vomiting, and abdominal pain. While very rare, severe rash can be accompanied by fever and/or elevations of liver enzymes, and can be life-threatening. Seek immediate medical attention. IRIS (immune reconstitution inflammatory syndrome) may occur as the immune system regains strength; signs and symptoms from previous infections may occur soon after HIV treatment is initiated. Report symptoms of illness, such as shingles or TB, to a health care provider. Protease inhibitors can cause increased risk for bleeding in hemophiliacs. Measure liver function before starting darunavir and then monitor. 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. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are many other drug interactions not listed here.

DR. MELANIE THOMPSON: Darunavir is coformulated in Symtuza. It has a high genetic barrier to resistance, meaning that a few missed doses are not likely to select for resistant viruses. But its Achilles' heel is that it requires boosting with ritonavir or cobicistat. That is one of the key reasons that darunavir-based regimens are not recommended for initial therapy for most people. A large observational study found darunavir to be associated with higher cardiovascular risk than atazanavir. Ritonavir should be used as a booster in pregnancy. Boosted darunavir taken with TAF or TDF and FTC or 3TC may be used when HIV is acquired after cabotegravir PrEP exposure and when an INSTI genotype result is not available at the time of initiation of therapy. Keep in mind that pill burden is important, and coformulated regimens may be preferable if cost allows.

ACTIVIST JOEY WYNN: Once a strong first line option, now it is 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.

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. Monitoring is recommended with buprenorphine, buprenorphine/naloxone, and methadone.

PREZCOBIX: Do not take with carbamazepine, dexamethasone, phenytoin, or phenobarbital, or with colchicine (in people with kidney or liver impairment). Not recommended to be taken with betamethasone, budesonide, ciclesonide, everolimus, fluticasone, Mavyret, methylprednisolone, mometasone, rifapentine, salmeterol, ticagrelor, triamcinolone, or voriconazole. Monitor for lack of virologic response when eslicarbazepine or oxcarbazepine is needed. Initiation or dose adjustments of insulin or oral hypoglycemic medications may be required for some individuals. Apixaban dose may need to be adjusted.

MORE INFORMATION

Darunavir is found in the single-tablet regimen Symtuza (see that page). The DHHS recommendation is "in part because of greater tolerability" with the integrase inhibitor medications. 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 IS AVAILABLE

Evotaz

300 mg atazanavir, 150 cobicistat
ATV (PI), COBI (PKE)

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

✔ Each is DHHS recommended as a component of initial regimen in certain clinical situations

STANDARD DOSE

REYATAZ: For most treatment-naïve (first time on HIV therapy) and treatment-experienced individuals, the dose is one 300 mg capsule + 100 mg Norvir or 150 mg Tybost once daily with food. See package insert for dosing recommendations during pregnancy, liver or kidney impairment, and with certain drug interactions. Capsules also available in 150 mg and 200 mg. Take Norvir or Tybost at 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

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

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.

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 recommendations. If taking chewable antacids, take with food two hours before or one hour after atazanavir dose. Treatment-experienced people should not take atazanavir with efavirenz. Tenofovir DF decreases levels of atazanavir, and Reyataz/Norvir increases tenofovir DF levels; monitor for adverse events. Monitoring is required when used with warfarin. Calcium channel blockers should be monitored. Reducing dose and frequency of rifabutin to 150 mg every other day or three times a week is recommended. Reyataz/Norvir as well as Evotaz increase levels of fluticasone; monitor for signs of Cushing's syndrome. An alternative corticosteroid is recommended. Erectile dysfunction drugs should not exceed 10 mg Cialis or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours. A lower dose of trazodone is recommended. Use with caution with bosentan, salmeterol, and immunosuppressants. Do not take with Zepatier. Can be used with Harvoni if tenofovir DF is not part of the HIV regimen. Monitor for tenofovir toxicities with Epclusa if TDF is part of the HIV regimen. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are many other drug interactions not listed here.

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

EVOTAZ: Do not take with lurasidone, pimozide, ranolazine, or dronedarone. Do not take with colchicine if there is kidney or liver impairment. Start metformin at lowest dose and titrate based on tolerability and clinical effect.

DR. MELANIE THOMPSON: Atazanavir-based regimens are not often used these days because of the high incidence of jaundice due to indirect hyperbilirubinemia (high bilirubin in the blood) and an increased risk of kidney and gallbladder stones, as well as kidney toxicity. They are not recommended for initial therapy in most people. 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 between atazanavir and cardiovascular disease. Unboosted atazanavir is FDA-approved for people who have not taken treatment before, but it is not recommended for initial therapy by DHHS or IAS-USA guidelines panels. In pregnancy, atazanavir 400 mg must be used with ritonavir as a booster. Evotaz is atazanavir coformulated with cobicistat and cannot be used in pregnancy (see Tybost). The monthly wholesale acquisition cost for Reyataz 300 mg is $1,449 and for Evotaz is $1,605, while generic atazanavir 300 mg ranges from $178 to $1,018.

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

MORE INFORMATION

Yellowing of the eyes is a common reason for discontinuation.

MANUFACTURER

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

REYATAZ AWP

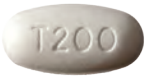
200 mg, 60 capsules:
$1,755.91/month
300 mg, 30 capsules:
$1,739.30/month

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")

▼ DHHS recommended for treatment-experienced people

■ GENERIC IS AVAILABLE

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

MORE INFORMATION

For people who have had virologic failure on an NNRTI-containing regimen, do not use Intelence in combination with a nucleoside backbone alone. Although taking once daily is not FDA approved, some providers have prescribed Intelence once daily (two of the 200 mg tablets) based on clinical trials that showed that once-daily Intelence was not inferior to Sustiva-based regimens. In Europe, it is approved as a once-daily medication. Once-daily dosing may improve adherence. Although the DHHS recommendation for Intelence specifies drug resistance strains before taking it, the drug label does not—you do not need to have drug resistance before taking Intelence. The TRIO study reported the combination of Intelence with Prezista/Norvir and Isentress in highly treatment-experienced people was successful in getting many people to undetectable. Some people complain of hard-to-swallow, large chalky pills; see dissolving instructions in dose section or package insert. For individuals with HIV-2, commonly found in some other countries, an NNRTI would not be recommended, as HIV-2 is inherently resistant to NNRTIs. DHHS guidelines do not recommend using etravirine in treatment-naïve people who are pregnant. Individuals who become pregnant while taking etravirine may continue taking Intelence if viral suppression is effective and the regimen is well tolerated. The pharmacokinetics (PK) of etravirine are not significantly altered during pregnancy, and no dosage adjustment is necessary. The PK data demonstrated that exposure to total etravirine was generally higher during pregnancy compared with postpartum levels. Etravirine is known to have a variable (moderate to high) level of transfer across the human placenta, although insufficient data exist to evaluate the effects on a fetus. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

DR. MELANIE THOMPSON: Etravirine was never approved for initial therapy and largely has been superseded by rilpivirine and doravirine, both of which can be taken once daily with lower pill burden and many fewer drug interactions. It 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, or 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 in 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")

✔ DHHS 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 or equal to 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.

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

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

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

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Edurant is a very tolerable medication. Moderate to severe side effects are uncommon. Most common side effects occurring in 3–5% of study subjects were insomnia, headache, rash, and depressive disorders. Stop taking Edurant and see a medical provider right away if allergic reaction or rash occurs with any of the following: fever, trouble breathing or swallowing, blisters, mouth sores, redness or swelling of the eyes, or swelling of the face, lips, mouth, tongue, or throat. Tell your doctor right away if you experience feelings of sadness, hopelessness, anxiety or restlessness, or have suicidal thoughts or actions. A small study showed a higher rate of depressive disorders in adolescents (19.4%—seven out of 36 youths—vs. 9% for adults), which may or may not have been related to Edurant. Edurant also has minimal negative effects on LDL ("bad") cholesterol, total cholesterol, and triglycerides compared to Sustiva. Edurant improved HDL ("good") cholesterol slightly less than Sustiva. Liver problems can occur, but are very rare. The risk may be greater for people with a history of hepatitis B or C, but may occur in people without a history of liver disease. Edurant can cause an increase in kidney function test (serum creatinine) within the first four weeks of treatment. The changes are not considered clinically relevant.

POTENTIAL DRUG INTERACTIONS

Edurant cannot be taken with the antiseizure medications carbamazepine, oxcarbazepine, phenobarbital, or phenytoin; the anti-TB drugs rifampin and rifapentine; proton pump inhibitors (Aciphex, Dexilant, Nexium, Prevacid, Protonix, and Prilosec); or St. John's wort. Do not take with more than one dose of the injectable steroid dexamethasone (sometimes given in the ER or hospital). Antacids or other products containing aluminum, calcium carbonate, or magnesium hydroxide should be taken two hours before or at least four hours after Edurant. Acid-reducing drugs (Pepcid, Tagamet, Zantac, and Axid) should be taken 12 hours before or four hours after an Edurant dose. If administered with rifabutin, the dose of Edurant should be increased to two 25 mg tablets once daily with a meal. When rifabutin is stopped, Edurant dose should be decreased to 25 mg daily. Monitor for worsening of any fungal infections when Edurant is used with antifungal medications such as fluconazole, itraconazole, ketoconazole, posaconazole, and voriconazole; dose adjustment for these medications may be needed. Use azithromycin when possible instead of clarithromycin, erythromycin, and telithromycin. Methadone levels are reduced slightly and people should be monitored for symptoms of withdrawal. Edurant should be used with caution when taken with other medications with a known risk for torsades de pointes or QT prolongation (these abnormal heart rhythms can make the heart stop).

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 taken once a month or once every two months; see Cabenuva. Edurant is not DHHS recommended for treatment-naïve people with a pre-treatment viral load greater than 100,000 copies/mL and CD4 T cell count below 200 cells/mm^3. The CD4 requirement, however, is no longer on the drug label. A rilpivirine-based regimen may be advantageous for people with high risk for heart disease due to its relatively low impact on lipid profile. The clinical benefit of these findings has not been demonstrated. While its tolerability and safety profiles are advantages for Edurant, the greater potential for virologic failure in people with high viral loads, food restrictions, and cross-resistance to the other NNRTIs puts Edurant at a disadvantage for first-time treatment—people may not be able to switch to another NNRTI if their HIV develops NNRTI-resistant mutations to Edurant. Data for use of rilpivirine in combination with an abacavir/lamivudine background are insufficient to recommend at this time. For individuals with HIV-2, commonly found in some other countries, an NNRTI would not be recommended as HIV-2 is inherently resistant to NNRTIs. Edurant can be used during pregnancy, and is listed as a DHHS alternative NNRTI to use during pregnancy in combination with a two-NRTI backbone. According to the FDA, lower exposures of rilpivirine were observed during pregnancy; therefore, viral load should be monitored closely. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$1,620.26/month

DR. MELANIE THOMPSON:

Oral rilpivirine is primarily used as a component of the STRs Odefsey, Complera, and Juluca. It should only be used when viral load is below 100,000 copies/mL and CD4 is at least 200 cells/μL 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 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; 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.

ACTIVIST JOEY WYNN:

Edurant is an NNRTI, 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 at this time; 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")

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

STANDARD DOSE

One 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. In the DRIVE-AHEAD study, an in-depth analysis examined the incidence of neuropsychiatric adverse events associated with a doravirine-containing regimen (Delstrigo) compared to Atripla. Neuropsychiatric events, such as depression, sleep disturbances, and dizziness, are another common side effect of NNRTIs. Doravirine did not appear to negatively affect cholesterol in studied populations.

POTENTIAL DRUG INTERACTIONS

When taken with rifabutin (used for TB and MAC treatment), increase the Pifeltro dose to one 100 mg tablet twice a day, approximately every 12 hours. The following are among the medications that may lower the blood levels of Pifeltro, and therefore may decrease its effectiveness, and should not be used with Pifeltro: the anticonvulsants carbamazepine, oxcarbazepine, phenobarbital, and phenytoin; the androgen receptor inhibitor enzalutamide; the antimycobacterials rifampin and rifapentine; the cytotoxic agent (cancer drug) mitotane; and the herbal St. John's wort. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions that are not listed here.

MORE INFORMATION

FDA approved in 2018, doravirine may be an option for people who have developed drug resistance to other NNRTIs. A single-tablet regimen (STR) containing doravirine was also approved in 2018; see Delstrigo page. Delstrigo, however, contains the older version of tenofovir, tenofovir DF. The standalone Pifeltro allows people to take it with the newer tenofovir alafenamide (TAF), found in Descovy, which has potentially less long-term renal and bone toxicity. On the other hand, TAF is associated with weight gain. Of course, the use of Pifeltro means the necessity for an extra pill, such as Descovy, or maybe more than one extra pill, depending on the regimen being used. Pifeltro was found to be non-inferior to boosted darunavir (Prezista) as well as efavirenz (Sustiva), with data now out to 96 weeks (2 years). Doravirine was superior to boosted darunavir at week 96 in terms of virologic suppression, but it should be noted there was a higher rate of study discontinuation in the boosted darunavir group. Doravirine is a non-nucleoside medication, and it should be noted that this drug class typically has a lower barrier to resistance, as well as extensive cross-resistance. Additionally, the emergence of resistance at the time of virologic failure has been reported with doravirine. Doravirine has tolerability advantages over efavirenz and has relatively favorable lipid effects when compared to both boosted darunavir and efavirenz. It also has fewer potential drug interactions than efavirenz or rilpivirine, and, unlike rilpivirine, virologic efficacy is not compromised among people with high baseline viral loads or low CD4 counts. Doravirine has not yet been directly compared to integrase inhibitor-based regimens in clinical trials. In a new DHHS statement last year, "In a cross-trial analysis, DOR was not associated with weight gain compared with [efavirenz] 600 mg or boosted [darunavir]." For individuals with HIV-2, commonly found in some other countries, an NNRTI would not be recommended as HIV-2 is inherently resistant to NNRTIs. No adequate human data are available yet to establish whether or not Pifeltro poses a risk to pregnancy outcomes. 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 never tested head-to-head against INSTIs, therefore is not recommended for first-line therapy in most circumstances. 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 that developed drug resistance to other NNRTIs. Pifeltro allows people to take it with other newer combinations. In resource constrained jurisdictions, this mediocre option may save the bank if it is limited in funding.

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")

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

■ GENERIC IS AVAILABLE

STANDARD DOSE

One tablet once daily on an empty stomach, preferably at bedtime (food can increase the risk of central nervous system, or CNS, side effects). 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. For children weighing less than 88 pounds (40 kg), the dose is based on weight. See package insert for specific weight-based dosing. For children weighing at least 88 pounds, use the standard adult dose. For those who can't swallow capsules, administer by capsule sprinkle method. See drug label for instructions or watch the video at sustiva.com.

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

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

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Central nervous system (CNS) side effects (dizziness, insomnia, impaired concentration, abnormal or vivid dreams, and hallucinations) are most common at the start of treatment and usually diminish in two to four weeks. Bedtime dosing on an empty stomach can help reduce symptoms. Less common psychiatric symptoms (catatonia, depression, suicidal thoughts or actions, aggression, paranoid/manic reactions) may also occur. A 2014 study reviewed four previously published AIDS Clinical Trials Group (ACTG) studies regarding efavirenz and suicidal ideation and re-emphasized efavirenz has an association with suicidality (reported suicidal ideation or attempted or completed suicide), and should be used with caution in people with severe or uncontrolled depression and/or a history of suicidality. It is recommended for anyone on a regimen containing efavirenz to be regularly screened for depression and suicidality. Additional side effects may include rash (incidence of up to 26% of adults and 32% of pediatric patients), nausea, vomiting, diarrhea, fever, and gynecomastia (breast development in men). Rash among children is more common and more severe. Efavirenz may raise levels of triglycerides (fat in the blood) and cholesterol. Efavirenz can cause a false positive for marijuana on certain drug tests. A more specific confirmatory test can be done. A link to birth defects in humans was not supported by meta-analyses. Individuals in their first trimester of pregnancy are recommended to continue taking efavirenz as long as their viral load remains undetectable; however, efavirenz should only be used if the potential benefit outweighs the potential risk, as when other treatment options are not available. Because of the association with suicidality and neuropsychiatric effects, it is also recommended to screen for antenatal and postpartum depression in women with HIV who are taking a regimen containing efavirenz. Regular monitoring for increased liver enzyme levels is recommended initially and during treatment for people with hepatitis B/C or liver disease.

POTENTIAL DRUG INTERACTIONS

Do not take with midazolam, pimozide, ergot derivatives, St. John's wort, or triazolam. May affect warfarin levels. Can decrease levels of buprenorphine and methadone—monitor for withdrawal. Increase Kaletra to two 200/50 mg tablets + 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, Lipitor, Pravachol, and Zocor doses may need to be adjusted. Titrate dose of bupropion and sertraline based on clinical response. Should not be taken with other medications that prolong QT interval (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 recommended for initial therapy 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 taken with TDF or TAF + FTC or 3TC. There is little rationale for prescribing efavirenz-based regimens at this time. It is still recommended during pregnancy, but data from IMPAACT 2010 show more frequent growth stunting with efavirenz than with dolutegravir.

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 currently.

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")

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

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. New TAF information as of 2022: "Post-marketing cases of renal [kidney] impairment, including acute renal failure, proximal renal tubulopathy (PRT), and Fanconi syndrome have been reported with TAF-containing products; while most of these cases were characterized by potential confounders that may have contributed to the reported renal events, it is also possible these factors may have predisposed people to tenofovir-related adverse events." At initiation and during treatment, assess kidney lab tests: serum creatinine, estimated creatinine clearance, urine glucose, and urine protein. In people with chronic kidney disease, also assess serum phosphorus. Discontinue Descovy in people who develop clinically significant decreases in kidney function or signs of Fanconi syndrome. Tell your provider about any pain in extremities, persistent or worsening bone pain and fractures, with or without muscular pain or weakness, as well as any concerning changes in urinary habits as these could be signs of bone or kidney problems. 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 or Temixys, Emtriva, Epivir-HBV, Hepsera, Truvada, Viread, or Vemlidy (TAF), used for the treatment of hepatitis B. Use caution with drugs that negatively affect the kidneys, including chronic use or high doses of anti-inflammatory drugs for pain such as Advil or Motrin (ibuprofen) and Aleve (naproxen). Descovy should not be taken with certain anticonvulsants (including carbamazepine, oxcarbazepine, phenobarbital, and phenytoin), Aptivus/Norvir, rifabutin, rifampin, rifapentine, or St. John's wort. Can be used with hepatitis C drugs such as Epclusa, Harvoni, or Zepatier. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions that are not listed here.

MORE INFORMATION

Descovy is similar to Truvada, except that instead of TDF (tenofovir disoproxil fumarate), Descovy contains TAF (tenofovir alafenamide), which reduces serum tenofovir concentration by up to 90%. This results in a decreased impact on kidney and bone demineralization but maintains potent antiviral activity in the CD4 cell. In clinical trials, fewer kidney and bone issues were observed with TAF than with TDF, and significant improvements were observed when switching from TDF to TAF. The long-term impact of TAF on people with osteopenia or osteoporosis is unknown. Both Descovy and Truvada are currently recommended by DHHS HIV treatment guidelines for first-time therapy for most people—in fact, one or the other combination is found in some of the single-tablet regimens. Descovy can be used for HIV prevention; see "Descovy for PrEP" page. Because both FTC and TAF are also active against hepatitis B (HBV), Descovy is recommended by DHHS for individuals co-infected with both HIV and HBV. Pediatric HIV guidelines recommend Descovy as part of a preferred regimen. TAF is an alternative NRTI for use in pregnancy, according to DHHS perinatal guidelines. Descovy tablets are relatively small compared to Truvada and other combination tablets, which may be helpful to people who have difficulty swallowing. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$2,590.94/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 who are not taking ritonavir or cobicistat. LDL and HDL cholesterol and weight gain are higher with Descovy than Truvada. Like Truvada, Descovy is active against hepatitis B, owing to the activity of both TAF and FTC.

Because of data from IMPAACT 2010, TAF/FTC is now recommended with dolutegravir as preferred drugs in pregnancy by the DHHS perinatal and adult guidelines panels and the IAS-USA panel.

The monthly wholesale acquisition cost of Descovy is $2,039.

ACTIVIST JOEY WYNN: Although smaller and easier to swallow than its predecessor, both backbone therapies have some side effect profiles for a small percentage of those taking it. Those side effects are often overstated and exaggerated, but 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 DHHS 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 EPIVIR.
➤ 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. 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.

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. Epzicom is recommended by DHHS as one of the preferred NRTI combination components of HIV treatment in pregnancy. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

DR. MELANIE THOMPSON: Ziagen and Epzicom are now generic. As a result, ViiV will discontinue brand name Epzicom and Ziagen tablets as of January 1, 2024 and stopped its patient assistance program for these products in July 2022. Abacavir has been an important medication, but always problematic. An obstacle for abacavir-containing regimens is the need to screen for the genetic marker HLA-B*5701 before dosing to avoid potentially life-threatening abacavir hypersensitivity. 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." DHHS guidelines recommend avoiding abacavir in persons with, or at high risk for, cardiovascular disease, and IAS-USA guidelines have removed Triumeq as recommended initial therapy partly because of these concerns. When abacavir is used with efavirenz or atazanavir + ritonavir, viral load should be 100,000 copies/mL or below. In early clinical trials, the most common side effects with abacavir were nausea, headache, malaise and fatigue, vomiting, and dream/sleep disorders. Abacavir is mainly used for people who can't take tenofovir-containing regimens, although 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.

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 IS AVAILABLE

Epivir

150 or 300 mg lamivudine
3TC (NRTI)

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

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

GENERIC IS AVAILABLE

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 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 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). Epzicom is recommended as a preferred initial regimen in pregnancy. Epivir as part of the combination tablet Combivir is recommended as an alternative NRTI combination component of an HIV treatment regimen during pregnancy. Epivir is available as generic lamivudine, which should be as effective and well tolerated as the brand name drug Epivir. 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.

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

DR. MELANIE THOMPSON: Emtricitabine, also called FTC, is similar to Epivir, also called lamivudine or 3TC, including in their resistance profiles. Their signature mutation, M184V, causes loss of antiviral activity but also increases the activity of tenofovir or AZT. They are considered interchangeable by guidelines panels for treatment, but not for prevention. 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.

The monthly wholesale acquisition costs are as follows: Emtriva $537; Epivir $416; generic 3TC $75 to $343.

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

Truvada

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

■ GENERIC IS AVAILABLE

Cimduo *and*  Temixys

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")

★ All are DHHS recommended as a component of initial regimen for most people

Viread

300 mg tenofovir DF
TDF (NRTI)

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

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

■ GENERIC IS AVAILABLE

STANDARD DOSE

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

➤ **SEE ALSO:** Emtriva and Epivir.

➤ **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 be seen with Cimduo and Temixys. 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. 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.

DR. MELANIE THOMPSON: TDF has a high genetic barrier to resistance and potent activity against hepatitis B. It is generally taken with FTC or 3TC as Truvada, Cimduo, and Temixys. Cimduo and Temixys include 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. While diarrhea, nausea and fatigue were the most common side effects seen in early clinical trials, side effects of highest concern include a potential for kidney toxicity, mostly mild but occasionally serious, and decrease in bone density. Serious toxicities are most often seen in people with other risks for kidney disease or low bone density, including older age or comorbidities, or when taken in combination with the boosters ritonavir or cobicistat. TDF also lowers LDL and HDL cholesterol and is associated with a bit of weight loss. TDF/FTC is safe in pregnancy. Generic TDF/FTC has been around since 2020 in the U.S., but only at a very high price, barely less than that of Truvada. Now, however, generic TDF/FTC is available from multiple manufacturers and may be priced as low as $25–35 per month.

ACTIVIST JOEY WYNN: Truvada does not have a negative impact on cholesterol levels and weight. At one point over 75% of people on therapy had a Truvada-based component in their regimen for over 10 years, so most people do not experience the side effects seen in a few. Cimduo and Temixys are hybrids between generic and brand medicines, and definitely have a niche inside the private insurance payor world. The optimal groups to use this would be benefiting people during pregnancy and those seeking an NRTI therapy. Neither is approved for PrEP at this time, but would be worth the effort to make it happen.

MORE INFORMATION

Don't believe the lawsuit advertisers: Truvada (and TDF) is a safe medication to take. 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
Temixys: $1,020.00/month

Norvir ritonavir RTV

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

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

■ GENERIC IS AVAILABLE

STANDARD DOSE

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

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

Approved for children older than one month with dosing based on body surface area; the use in children depends on the co-administered PI. Capsule formulation requires refrigeration, but the tablet does not. Liquid formulation available (80 mg/mL) in peppermint caramel flavor, but 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 pain, nausea, diarrhea, and vomiting. Other less common side effects may include fatigue; tingling/numbness around the mouth, hands, or feet; loss of appetite; and taste disturbances. Norvir can also increase cholesterol and triglyceride levels. Measure liver function before starting and then monitor, with perhaps closer monitoring for those with underlying liver problems, especially during the first several months. No dose adjustment necessary with mild to moderate liver disease, but Norvir is not recommended for those with severe liver impairment.

POTENTIAL DRUG INTERACTIONS

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

DR. MELANIE THOMPSON: Ritonavir is 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. 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 has recently updated its prescribing checklist and drug interaction guide for Paxlovid: www.fda.gov/media/158165/download. HIVMA and IDSA have updated their recommendations here: idsociety.org/globalassets/covid-19-real-time-learning-network/patient-populations/hiv/oral-covid-tx-considerations-for-people-with-hiv-and-hcv.pdf. The NIH COVID-19 and treatment guidelines address Paxlovid here: covid19treatmentguidelines.nih.gov/therapies/statement-on-paxlovid-drug-drug-interactions/.

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—however, some other HIV medicines should not be taken with high-fat foods.

MANUFACTURER

AbbVie
norvir.com; (800) 633-9110

AVERAGE WHOLESALE PRICE

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

Tybost

150 mg cobicistat
COBI (PK booster)

PKE **Pharmacokinetic enhancer (booster)**

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

STANDARD DOSE

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

For adults and children weighing at least 77 pounds (if taken with atazanavir, brand name Reyataz) or at least 88 pounds (if taken with darunavir, brand name Prezista or in the single-tablet regimen Symtuza; anyone taking darunavir must be at least three years old). Tybost is not an HIV drug; it is a pharmacokinetic enhancer or a "booster" used to increase the levels of Prezista 800 mg once daily, Reyataz 300 mg once daily, or elvitegravir 150 mg in Stribild and Genvoya. Tybost is not interchangeable with Norvir when used to increase the levels of other HIV medications.

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

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Side effects observed in clinical studies (greater than 2% of people) include rash, jaundice, and yellowing of the eyes. However, it was studied with Reyataz so the jaundice and yellowing of eyes were most likely due to the Reyataz component. Before taking Tybost, kidney function testing should be conducted, including serum creatinine (SCr), serum phosphorus, urine glucose, and urine protein. These measurements should continue to be monitored while taking Tybost. Cobicistat can cause a small, reversible increase in serum creatinine within the first few weeks of treatment without affecting actual kidney function. While cobicistat does not affect actual kidney function, its effect on SCr can make monitoring of impaired kidney function more difficult or less accurate.

POTENTIAL DRUG INTERACTIONS

Tybost is not interchangeable with Norvir. Tybost interacts with many drugs. Do not take with alfuzosin, colchicine, dihydroergotamine, dronedarone, ergotamine, irinotecan, simvastatin, lovastatin, lurasidone, methylergonovine, ranolazine, rifampin, pimozide, triazolam, oral midazolam, Revatio, or St. John's wort. Tybost may increase levels of nasal or inhaled fluticasone (Flonase, Advair, Breo Ellipta, Arnuity Ellipta, and Flovent). Use an alternative corticosteroid and monitor for signs of Cushing's syndrome (increased abdominal fat, fatty hump between the shoulders, rounded face, red/purple stretch marks, increased appetite, bone loss, possible high blood pressure, and sometimes diabetes). No significant interactions with beclomethasone. Tybost may increase levels of certain calcium channel blockers, beta blockers, HMG-CoA reductase inhibitors (statins or cholesterol medicines), anticoagulants, antiplatelets, antiarrhythmics, antidepressants, sedative-hypnotics, rifabutin, bosentan, erectile dysfunction agents, inhaled corticosteroids, and norgestimate. Caution should be taken, with possible dose adjustments of these medications, when used with Tybost. Sporonox (antifungal) and Biaxin (antibiotic) may increase Tybost concentrations. Tybost may also increase Biaxin levels. Rifabutin and some anti-seizure medications, such as carbamazepine (Tegretol), phenobarbital, and phenytoin (Dilantin) may decrease Tybost drug levels. Start metformin at lowest dose and titrate based on tolerability and clinical effect. Do not take with Olysio, Viekira Pak, or Zepatier. Avoid Harvoni if tenofovir disoproxil fumarate (TDF) is part of the HIV regimen. Tybost has 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 the other booster. Simply say, "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 DHHS treatment guidelines for use in certain clinical situations. Tybost shares some of the same side effects, such as increased cholesterol and increased triglycerides, as Norvir; however, in clinical trials they were less pronounced. Tybost co-administered with elvitegravir, darunavir, or atazanavir should not be initiated in pregnant individuals and is not recommended during pregnancy. Inadequate levels of ART (antiretroviral therapy) in second and third trimesters as well as viral breakthroughs have been reported. Tybost is not recommended during pregnancy. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$339.96/month

POSITIVELY AWARE

For pagination purposes, this page has been intentionally left blank.

For pagination purposes, this page has been intentionally left blank.

POSITIVELY AWARE

For pagination purposes, this page has been intentionally left blank.

Apretude

cabotegravir extended-release injectable suspension
CAB LA

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.

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. Longer needles, two inches (not included in the dosing kit), may be required for people with a higher BMI (body mass index) of 30 or more.

- Oral cabotegravir is not available unless being prescribed cabotegravir LA.
- SEE PACKAGE INSERT for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

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

POTENTIAL DRUG INTERACTIONS

Cabotegravir cannot be taken with rifampicin, rifapentine, carbamazepine, oxcarbazepine, phenytoin, and phenobarbital. It is recommended to co-administer rifabutin with caution because rifabutin can moderately increase the metabolism of cabotegravir and result in lower protective levels of cabotegravir. The effect of feminizing medications and hormones 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. New options are highly desirable—different strokes for different folks. According to PrEP guidelines from the U.S. Centers for Disease Control and Prevention (CDC), "Cabotegravir injections may be especially appropriate for people with significant renal disease, those who have had difficulty with adherent use of oral PrEP, and those who prefer injections every 2 months to an oral PrEP dosing schedule." 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 if HIV is acquired after stopping medication and the drug is still leaving the body, and the importance of keeping up follow-up appointments if stopping PrEP for any reason. DHHS guidelines have a section on the use of cabotegravir LA for people with a history of injection drug use. Apretude is not recommended for people who are pregnant. Because cabotegravir LA has been detected in systemic circulation for up to 12 months or longer after the last injection, consideration should be given to potential for fetal exposure if prescribing cabotegravir to people of child-bearing potential who are not on birth control. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

DR. MELANIE THOMPSON: In clinical trials, Apretude was superior to oral Truvada in preventing new HIV infections among gay and bisexual men and transgender women, and for cisgender women. Injection site reactions were very common but rarely caused anyone to stop taking the drug. Because the risk of missing an acute HIV infection when starting CAB PrEP could result in cross-resistance to all integrase inhibitors and limit treatment options, an HIV RNA viral load test is required before every dose of CAB. 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, 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), DHHS 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. In spite of concerns about drug resistance, 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 populations. This is a heavy lift. A great deal of public and provider education is needed, and the high cost of the drug (wholesale acquisition cost of $3,700 per dose) as well as the operational logistics of administration, are significant obstacles. Currently, oral PrEP must be provided to insured persons without out-of-pocket costs due to its "A" rating from the U.S. Preventive Services Task Force (USPSTF). At the time of publication, USPSTF was in the process of updating its recommendations to include CAB PrEP. To facilitate uptake with equity, the drug as well as its administration costs and associated labs must be fully covered without cost sharing, and without forcing people to take an oral option instead. People with no insurance or inadequate insurance may be able to access the drug through ViiV's patient assistance program, but must have a prescription from a care provider. It's too soon to know how the roll out of Apretude will go, but advocates should follow closely using an equity lens to ensure that all persons have convenient and equity-based access to all available PrEP options. In addition, a recent court ruling eliminates the requirement that insurers pay for PrEP and PrEP-related services creates a new barrier and should be addressed legislatively.

ACTIVIST JOEY WYNN: Studies found Apretude to be superior to Truvada in preventing HIV acquisition. Apretude is an injection, so this is not for everyone. This revolutionary formulation will have a huge impact in dramatically reducing new cases of HIV in the U.S. Barriers removed can include the burden of taking pills and going to the pharmacy for pick up, co-pay costs, and all the other headaches of getting and taking pills. Now we will get to see a majority of folks staying on their PrEP year round.

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)

★ 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 who took 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, 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. 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/basics/prep.html. Gilead Sciences helps people work with their insurance, including pre-authorizations, as well as provides free PrEP to uninsured people who are eligible and co-pay assistance for insured individuals up to $7,200 a year; contact the patient assistance hotline 24/7 at (877) 505-6986, or GO TO gilead-advancingaccess.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 cis-women, people who inject drugs, and transgender men, and consequently, Descovy is not approved for these populations, thus widening disparities. Gilead's PURPOSE-1 trial of Descovy vs. lenacapavir for PrEP is beginning in Africa for young cisgender women and girls. Luckily, Truvada remains the first choice for PrEP for many people, including cisgender women who are pregnant or contemplating pregnancy, and the price is decreasing over time owing to generic competition. 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. 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. 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. In addition, a recent court ruling eliminates the requirement that insurers pay for PrEP and PrEP-related services creates a new barrier and should be addressed legislatively.

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 PrEP services. Resources abound on how to get access to this and remove barriers to copays 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)

★ FDA approved for the prevention of HIV

■ GENERIC IS AVAILABLE, BUT NOT APPROVED FOR PrEP

STANDARD DOSE

For HIV-negative adults and adolescents weighing at least 77 pounds (35 kg), 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. Truvada should not be used for prevention if CrCl or eGFR (measures of kidney function) is less than 60 mL/min.

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

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

POTENTIAL SIDE EFFECTS AND TOXICITY

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

POTENTIAL DRUG INTERACTIONS

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

MORE INFORMATION

Truvada for PrEP is 99% effective in preventing HIV when taken daily as recommended. Stigma and lack of access to health care continue to fuel HIV infections. Remember, risk depends on the situation—including where you live. Other problems include not knowing about PrEP and inability to perceive a need for it (not realizing one may have vulnerabilities at all). Although the drug label specifies prevention of sexually-acquired infection, U.S. HIV guidelines also recommend use for protecting against infection through injection drug use (reducing the risk of HIV by more than 70%, according to the CDC). The label notes that risk includes a number of behavioral, biological, or epidemiological factors, including condomless sex, current or past STIs, self-identified risk, having sexual partners of unknown HIV status or unknown HIV viremic status, or sexual activity in a high prevalence area or network. Screening and monitoring requirements include checking for STIs and for hepatitis B and C. Insurers must 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 24/7 at (877) 505-6986, or GO TO gileadadvancingaccess.com. On-demand PrEP with Truvada, which uses four tablets around the time of sex, is supported by guidelines from the International AIDS Society-USA, the European AIDS Clinical Society (EACS), and the World Health Organization. Truvada generic became available in the U.S. in October 2020. See discussion online of the generic's pricing (positivelyaware.com/articles/briefly-novdec-2020 and positivelyaware.com/articles/briefly-jul-aug-2017). DHHS HIV guidelines have a section on using PrEP for periconception, antepartum, and postpartum periods. PrEP Facts: Rethinking HIV Prevention and Sex is a closed Facebook group for people interested in or currently on PrEP, and their allies. For more information, GO TO cdc.gov/hiv/basics/prep.html. Pregnant individuals can voluntarily enroll in the Antiretroviral Pregnancy Registry through their provider; GO TO apregistry.com.

DR. MELANIE THOMPSON: Truvada was approved for PrEP in 2012 after being shown to be highly effective when taken with excellent adherence. Generic TDF/FTC is now available at low cost in the US. (It should be noted that 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. The availability of generic TDF/FTC makes TDF-based PrEP the least expensive of all options. We badly botched the rollout of PrEP in the U.S., and far too many people who could benefit still lack access to PrEP, with wide disparities by race, ethnicity, and gender. We should learn from these mistakes and make all PrEP and PrEP services available at no cost by fully funding a national PrEP program, such as the one currently proposed by President Biden, and centering all programs on equity. In addition, a recent court ruling eliminates the requirement that insurers pay for PrEP and PrEP-related services creates a new barrier and should be addressed legislatively.

ACTIVIST JOEY WYNN: Truvada—although controversy abounds, this work horse has helped many a person maintain their viral load, and now 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 those contemplating pregnancy.

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)
tegriftasv.com/resources

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

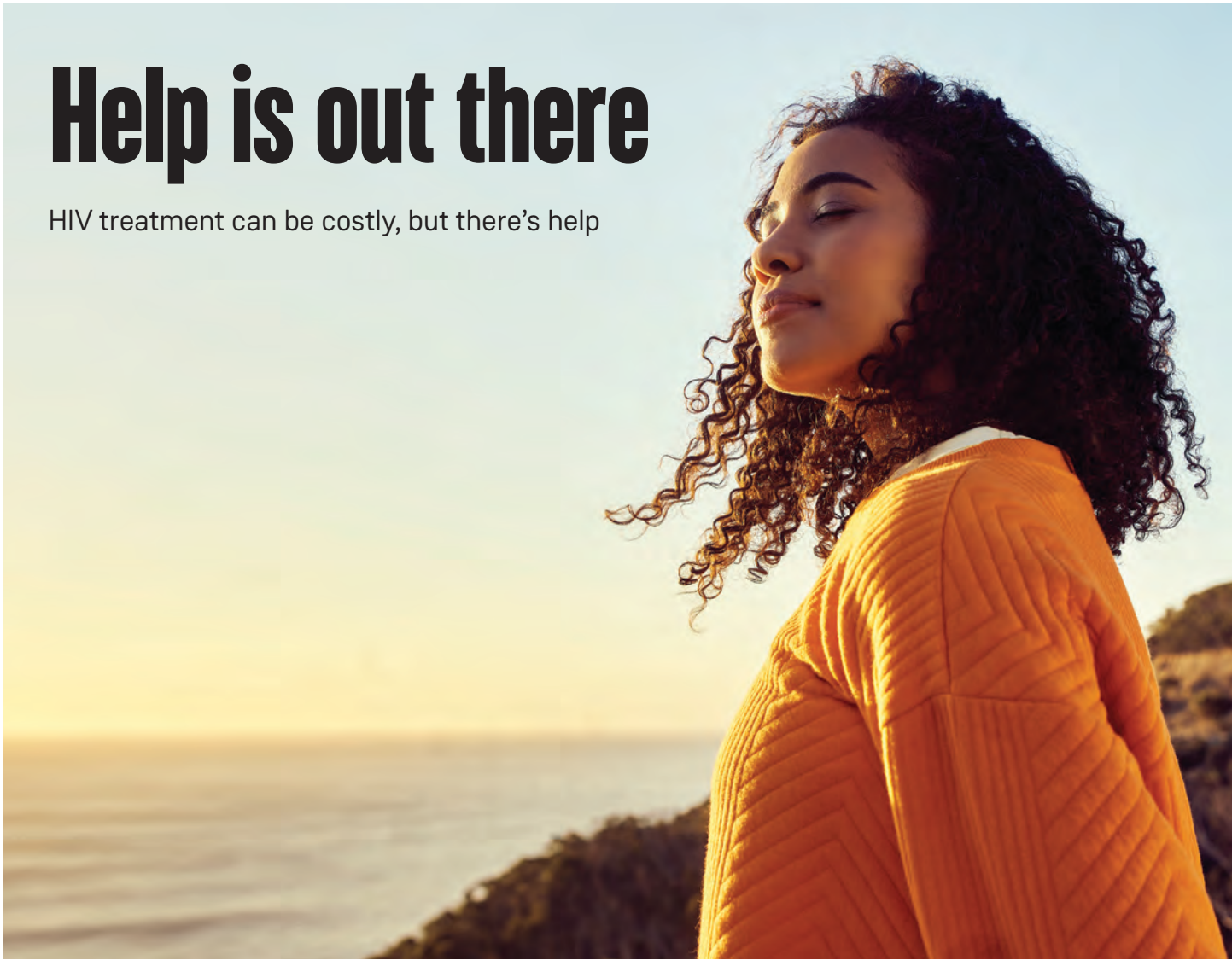
EMD Serono
serostim.com; (877) 714-AXIS (2947)

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

ISTOCK

in his or her state and is verified to be on an ADAP waiting list in that state.

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

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

INFORMATION IN THIS ARTICLE and the tables on the following pages are adapted from NASTAD's *HIV Pharmaceutical Company HIV Patient Assistance Programs and Cost-Sharing Assistance Programs:* bit.ly/hiv-cap-and-pap.

COST-SHARING ASSISTANCE PROGRAMS (CAP)

DRUGS COVERED	MANUFACTURER AND CONTACT INFORMATION	ASSISTANCE	RENEWAL
Kaletra and **Norvir**	**AbbVie** 800-441-4987, option 5; kaletra.com; norvir.com	**Kaletra:** Co-payment assistance covers up to the first $400 per prescription per month. **Norvir:** Covers up to $1,200 a year for co-payments.	
Atripla, **Biktarvy**, **Complera**, **Descovy**, **Emtriva**, **Genvoya**, **Odefsey**, **Stribild**, **Truvada**, **Tybost**, and **Viread**	**Gilead Sciences** 877-505-6986; gileadadvancingaccess.com	**Biktarvy, Descovy, Genvoya, and Truvada:** Covers the first $7,200 per year of co-payments. **Complera, Odefsey**, and **Stribild:** Covers the first $6,000 per year of co-payments. **Emtriva:** Covers the first $300 per month/$3,600 per year of co-payments. **Tybost:** Covers the first $50 per month/$600 per year of co-payments.	Rolls over on January 1
Edurant, **Intelence**, **Prezcobix**, **Prezista**, and **Symtuza**	**Janssen Therapeutics** 866-836-0114; janssencarepath.com; edurant.com; intelence.com; prezista.com; prezcobix.com; symtuza.com	Covers the first $7,500 per year (for Symtuza, it's $12,500) of co-payments, deductibles and co-insurance.	Automatic renewal
Delstrigo, **Isentress**, **Isentress HD**, and **Pifeltro**	**Merck and Co.** 800-444-2080; isentress.com	Covers the first $6,800 of co-payments, deductibles and co-insurance.	Enrollment is valid until coupon expires, 12/31/2023
Trogarzo	**Theratechnologies** 833-238-4372; trogarzo.com	Contact program for details Worked out on a case-by-case basis	
Cabenuva, **Dovato**, **Juluca**, **Retrovir**, **Rukobia**, **Selzentry**, **Tivicay**, **Tivicay PD**, **Triumeq**, **Trizivir**, **Viracept**, and **Ziagen**	**ViiV Healthcare** 844-588-3288; ViiVConnect.com	**Cabenuva,** $13,000; **Dovato** and **Juluca,** $6,250; **Tivicay,** $5,000; and **Triumeq** and **Rukobia,** $7,500 per year/per patient maximum. **Lexiva, Rescriptor, Retrovir, Selzentry, Trizivir, Viracept,** and **Ziagen:** $4,800 per year/per patient maximum.	Automatic renewal
Invirase and **Viread**	**Patient Access Network Foundation** 866-316-7263; panfoundation.org	Maximum benefit is $3,600 per year. Patients may apply for a second grant during their eligibility period subject to availability of funding. All HIV funds are closed. Can only get on a wait list.	Reapply each year

PATIENT ASSISTANCE PROGRAMS (PAP)

DRUGS COVERED	MANUFACTURER AND CONTACT INFORMATION	FINANCIAL ELIGIBILITY
Kaletra	**AbbVie** 800-222-6885 kaletra.com; abbviepaf.org	$81.540 600% FPL
Aptivus, Viramune XR	**Boehringer Ingelheim** 800-556-8317; boehringer-ingelheim.us	$72,000 (500% 2023 FPL)
Atripla, Biktarvy, Complera, Descovy, Emtriva, Genvoya, Odefsey, Stribild, Truvada, and **Tybost**	**Gilead Sciences*** 800-226-2056 gileadadvancingaccess.com	$67,950 (500% 2022 FPL)
Edurant, Intelence, Prezcobix, Prezista, and **Symtuza**	**Janssen Therapeutics** 800-652-6227; jjpaf.org	$40,770 (300% 2022 FPL)
Delstrigo, Isentress, Isentress HD, and **Pifeltro**	**Merck and Co.** 800-727-5400 merckhelps.com; isentress.com	$58,320 (400% 2023 FPL)
Trogarzo	**Theratechnologies** 833-238-4372; trogarzo.com	Call program for details
Apretude, Cabenuva, Combivir, Dovato, Epivir, Epzicom, Lexiva, Juluca, Rescriptor, Retrovir, Rukobia, Selzentry, Tivicay, Triumeq, Trizivir, Viracept, and **Ziagen**	**ViiV Healthcare** 844-588-3288; ViiVConnect.com	$67,590 (500% 2022 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.

ISTOCK

An HIV cure? **Not today**

Understanding the complexities of HIV and why a cure isn't coming soon is key to developing strategies for an eventual cure

BY **LYNDA DEE** AND **JEFF TAYLOR**

With more than half a century of advocacy work between them, **Lynda Dee** *and* **Jeff Taylor** *have spent the last decade pushing to develop a cure for HIV. They are community advisory board members and community engagement coordinators of the Martin Delaney Collaboratories for HIV Cure Research, an interdisciplinary collaboration funded by the National Institutes of Health comprised of basic, applied and clinical researchers in academia, community, government and industry working together to develop cure strategies for HIV. During an Introduction to* HIV Cure-Related Research *workshop, Dee and Taylor presented on the complexities of cure research. While an HIV cure won't be here tomorrow, understanding those complexities will someday lead to cure. But what do we mean when we say* cure*? Following are excerpts from their presentations.* **—RICK GUASCO**

Lynda Dee

The cure has to be scalable for eveyone

We have to say at the beginning that an HIV cure is not around the corner. We don't want people to think that *O.K. , we'll be cured tomorrow*. Science doesn't work that way.

What do we mean when we say *cure*? Does that mean that we're completely cured—eradication—that HIV is completely gone from someone's body? Or does it mean that HIV is controlled without daily drugs? Can we have the ability to control HIV without taking antiretroviral meds? We'd love to have a complete cure, but that will probably happen gradually, in stages, just like how antiviral therapies were developed. We didn't get to *one pill, once a day* overnight.

What kind of cure do we want? What are the requirements for a cure? We want it to be safe. We have drugs now that are relatively safe, that are one pill once a day, which is pretty simple. We want to be sure that we keep prices down so that everybody gets a chance to get these drugs, not just rich people or rich countries. An HIV cure has to be scalable. What do we mean by that? We mean that our brothers and sisters in developing countries will also have an opportunity to have these drugs, and the drugs won't be so complicated to make or use that it would be impossible to have access to them. We want the drug to be durable, which means it will work for a long period of time in your body.

Here are the reasons why we need optimized treatments and a cure for HIV. There are about 38 million people with HIV across the world. If people in the U.S. have difficulty accessing treatment, imagine how much harder it is in other countries. Now imagine having to overcome these challenges every day.

There's drug resistance, which means all of a sudden the virus

If people in the U.S. have difficulty accessing treatment, imagine how much harder it is in other countries.

overwhelmed the meds you've been taking and now they don't work anymore. This can happen for numerous reasons. Also, there are toxicities that can develop when you're taking medications for years, decades—not only for HIV, but for other illnesses and conditions.

Why do we need a cure? With HIV comes cardiovascular disease, which means heart attacks, which may result from inflammation caused by HIV. Premature aging and frailty, weaker bones, neurologic disorders and cancer can also occur. You might have developed a certain kind of cancer 10 years later in your life, but you get it earlier now because your immune system is compromised. You have diabetes because maybe you have a propensity to that, but maybe the drugs are causing it to happen sooner. Lipodystrophy, the redistribution of body fat that we've also seen affect people's faces, has been caused by HIV drugs. A lot of this is immune exhaustion. We still haven't been able to determine the root causes of a lot of this—whether it's the drugs doing this, or the HIV or if it's a combination of both.

Why do we think a cure for HIV is possible? As of right now, there are five people who have been cured from HIV: Timothy Ray Brown, who maybe many of you have heard of, who was cured but eventually died because his cancer came back, not because of his HIV. Adam Castillejo, the London patient, has been cured. Marc, the Düsseldorf patient, has been cured for about 10 years. The New York patient, who is not yet ready to talk about their experience and the City of Hope patient, who came out at the last IAS [International AIDS Society] meeting. None of them were cured in a way that relates to most people though. They had cancer. They had chemotherapy, cancer treatment that didn't work for them until they underwent a very risky stem cell transplant operation. Doctors transplanted new immune systems into their bodies, essentially transplanting cells that were immune to HIV.

Timothy's doctors realized he was cured of HIV as well as cancer by essentially giving him a new immune system that can't be infected by HIV because he received a different type of CCR5 cell that is resistant to HIV. The key that opens the door to HIV entering his body was removed. This strategy has also been used successfully for other patients with HIV and cancer. We don't know if their cancer will come back, but they have been cured of HIV. Unfortunately, this strategy is not for everyone. The patients with HIV and cancer risked death because cancer was killing them. This is obviously not an option for people who do not have cancer. But the point is, if we can cure people living with HIV who also have cancer, we hope that means we can find a cure for people with HIV, using different strategies, even though it is different and will take us a long time and a lot of research to figure out how to do it.

Jeff Taylor

Finding a strategy to outsmart a clever virus

Why is it so hard to cure HIV? The answer is the reservoir where HIV hides out. If you take your HIV meds, you stand a good chance of becoming undetectable. But that doesn't mean there's no virus in your body. It just means that it's not detectable in your blood. It's still hiding out in all these parts of your body—your brain, your lymph nodes, your stomach, bone marrow and the genital tract. If you stop your meds, the virus comes roaring back. That's the problem that they're trying to solve with HIV cure research therapy.

So, how are we trying to address this? What are we trying to do? There are a lot of different pathways. The first is called *latency reversing*, which is just a fancy term of saying you're going to wake up the virus. The virus is latent, dormant, asleep. It's not doing anything in your cells because it's suppressed in the bloodstream by the HIV medications that people take. So, the idea here is to wake that virus up, and then find a way to kill it. This is called *kick and kill*. It sounds a little violent, depending on how you feel about your virus. When the virus is in this dormant state, it gets incorporated or integrated into the blood cells and other cells in your body. The idea is to activate or wake them up, and that way the cells release the virus. Your body, or your medication, can recognize them and kill them. The cells will die, but so will the HIV. One of the downsides of this is that latency-reversing drugs are used in cancer treatment, and they can be really toxic. Another downside is that they don't wake all the HIV up. All it takes is one cell, and once you stop medication, eventually that cell will wake up and start releasing HIV. You haven't really cured HIV.

Another approach is to use your body's own defenses. We all have antibodies that fight different infections, and we have antibodies against HIV. The problem is that HIV is a clever virus. It mutates a lot and and finds ways around the antibodies, just like it did against HIV drugs in the early days when we only had one or two drugs until we developed a cocktail that could stop HIV in various ways and keep it suppressed. It's the same thing with antibodies. What researchers discovered is that there are people whose bodies did a better job suppressing the virus, and they had special antibodies that are called broadly neutralizing antibodies—bNAbs—because they can control more kinds of virus, and now they're combining them.

The bNAbs are taken from those people and are multiplied

outside the body in a test tube. They're put back into people with HIV to see if the right combination of broadly neutralizing antibodies can help suppress the virus. We've had some promise with this, and it may work in two different ways. It could be an effective non-drug therapy for people living with HIV. You would give them this treatment and it might work for a while, and eventually you might have to give them more, because the antibodies don't reproduce in the body. You're always having to administer the bNAbs, just like with a drug, giving people new ones all the time, unless you can find a way to get the body to produce its own antibodies. This will be a continual therapy. It might be considered a functional cure—you might have to take shots every year or so to make it work. But this is an approach that is being looked at both for long-acting therapy and possibly as a cure.

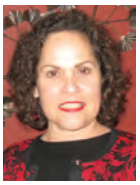
Lynda was talking about the five people who have been cured and so as she said, what they did was they basically gave them a new immune system and gave them new cells that could not be infected by HIV. But as Lynda said, that's not something anybody wants to do. That therapy can kill you. For Timothy and Adam, their cancer treatments were failing them, so it was a risk worth taking. But for the rest of us who were taking our meds and doing pretty well, that's not an acceptable risk.

I always tell people, *Yeah, it's great for those five people, but don't try this at home.* It's not anything you want to go through. And if you talk to any of them, they will tell you the horror stories of going through chemo and radiation or bone marrow or stem cell transplants. They got sick with something called graft versus host disease that people with transplants get because you're basically transplanting a new immune system into them. There are a lot of problems with this approach.

So, they're trying to find a kinder, gentler way of doing this. What they're doing is trying to modify the cells or the genes themselves to make this happen. There are a couple of ways to do this. One way is *ex vivo*, which just means outside the body. Cells are taken from someone living with HIV—T cells or stem cells from bone marrow—and they are modified in a test tube in a lab. Those cells are changed so that they cannot be infected by HIV. They're basically immune to infection. These special modified cells are then put back into a person's body. The idea is that these cells will incorporate themselves into your body, multiply on their own and be resistant to HIV infection. The new cells will take over and form a new immune system. Eventually, over time, these will take over HIV. It works really well except it's really complicated.

I won't go into it a lot but we hear a lot of news about things like CRISPR/Cas9 gene modification. They work like molecular scissors and just take your cells, cut out the parts that allow those cells to become infected by HIV so that it makes them resistant to infection. And then those cells are what are allowed to multiply either outside the body and are reinjected or used with a carrier virus to inject them into the body and multiply on their own and basically replace your immune system.

Another approach is to take advantage of what the the virus already does. What it does is it gets into a cell. And most of the time, as we said earlier, it just kind of stays there, especially if there's not virus multiplying in the blood. So, they have these long-term—they call it *quiesced* or *senescence*—cells that basically stay asleep. If you can just keep them asleep, you won't have sickness. You won't completely eliminate the virus from your body, but it won't do harm. And that's the next best thing. If we can do that, then we can call it a win, if it works effectively. The idea is to keep the cells from multiplying and reading the HIV DNA, because once that happens, the HIV takes over your immune system cells, starts to multiply and then causes infection and that's what makes you sick. If we can lock HIV's DNA from ever being read, you've solved the problem, and people stay healthy without having to take HIV medications. PA



LYNDA DEE is an HIV/AIDS treatment activist who co-founded AIDS Action Baltimore in 1987 after the death of her husband and two-thirds of her friends as a result of AIDS complications. She has worked for 35 years with academia, industry and government to expedite ethical drug development to provide access to life-saving medications before approval and to ensure reasonable drug prices and increases. She was co-chair of Martin Delaney Collaboratory (MDC) CARE CAB, co-chair of the MDC DARE CAB, co-chair of the amfAR Cure Institute CAB and is now the DARE MDC Community Engagement Coordinator.

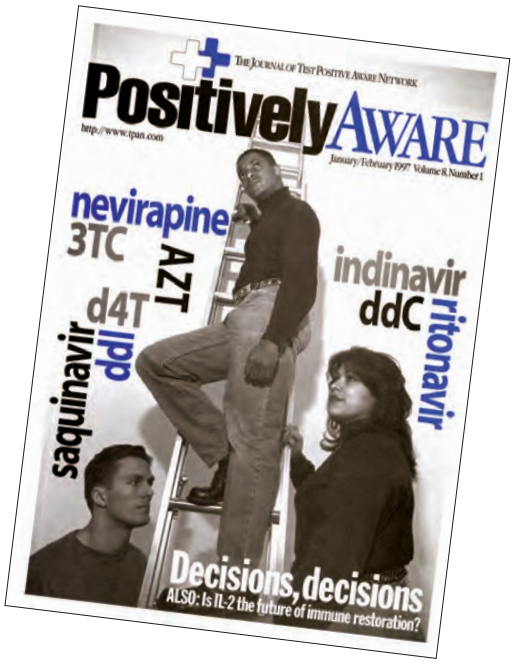
JEFF TAYLOR is a 60-year-old gay man who has been living with HIV for 40 years. He became involved in HIV research as a volunteer for the first AZT trials in 1988, and has been involved in HIV cure research for the past 15 years. He is currently the community engagement coordinator for the RID HIV Collaboratory for HIV cure research.

If we can lock HIV's DNA from ever being read, you've solved the problem, and people stay healthy without having to take HIV medications.

That was then, this is now

Twenty-seven years later, Sylvia and Sanford reflect on having appeared on the cover of our first HIV drug guide

BY **RICK GUASCO**



Living with HIV was very different in 1997, the year when the POSITIVELY AWARE annual HIV Drug Guide was first published. It was also early days for Sylvia O'Shaughnessy and Sanford E. Gaylord in their journey living with HIV when they agreed to be photographed for the cover of that first drug guide. (The third person on the cover was an HIV-negative model.)

Sylvia

"I wanted to educate everybody," Sylvia O'Shaughnessy says. "I especially wanted to educate women. I had this burning desire to let people know that you could live with this disease and still stay healthy. My thing was, don't stop living. A lot of us are alive, but we're not living. When you get diagnosed with HIV, that's basically what happens—you stop living, you're just alive."

Her children were supportive of her taking part in the cover shoot. It was in contrast to when O'Shaughnessy initially disclosed her status to her own parents. "She was very casual about it, but when I wet my hands and dried them with a towel, my mother made sure to immediately put the towel in the washing machine," she says. "The fact of the matter is back then I couldn't even blame her because I myself didn't know. I didn't know there was information out there. It was the early '80s; we didn't really have anyone to talk to."

Born into a Puerto Rican family (Sylvia is the younger sister of POSITIVELY AWARE associate editor Enid Vázquez), there were cultural issues as well. "As a Hispanic, we don't take our issues outside of our family," she says. "So, I didn't know of anything that was out there. At first it hurt. It was such a big hurt to see my mother doing this and to see how my family was walking on eggshells around me. But as the years went by, my parents grew to understand. My father started watching every news story about it. Back then there were a lot of stories about AIDS, they didn't even say HIV. My dad would tell my mother what he learned, and they started educating themselves from what my father was watching and reading. After a while, the tension that was at the beginning, was no longer there."

In the early days of the AIDS epidemic, HIV was usually considered a death sentence. "I sat around for years waiting to die because in the beginning, the doctor told me that in three months to six months, I was going to be gone and to put my kids up for adoption and get my affairs in order," she says. "I'll never forget that, the fear that they put in me with those words, the anger that I got towards God."

It challenged her faith. "How the hell do we have this loving God who would punish me—*what did I do?*" she says. "I couldn't understand. So, I became an atheist."

But as she lived beyond her initial prognosis, she came to another realization. "Doctors have an 'MD' after their name, but they're not God, so I let go of that fear. I lived past six months and then I lived past a year, so I started negotiating with God. *Let me live to see my daughter turn 12 years old, let me live to see my son go to kindergarten.* I kept bargaining for years. Today, I say, *Jesus Christ, you don't want me? What's taking you so long?* Old age has crept up on me, which I wasn't expecting. I was 23 when I was diagnosed; I didn't think I was gonna see 24. I'm past 60 now. I got diabetes, high blood pressure, high cholesterol. I'm going through a lot of old age shit. I never thought I would live this long and go through what I'm going through now."

Still, she reflects on what keeps her going. In addition to her three adult children, she has 11 grandchildren and three great-granddaughters. "There is so much that keeps me alive," O'Shaughnessy says, "I am grateful. I always learned the hard way. If things are too easy, you just don't know better and you take it for granted. HIV was the hard way of learning that I have to be living, not just be alive. I learned to live. Today, I do arts and crafts. I refinish and redo tables and furniture and paint them. I create. I enjoy life. I wake up every morning thanking God for another day of life. There are times when I'm really ill and really, really down. I look up and say, *God, what are we waiting for?* But I'm still here because I still got something else to learn; that's how I look at it. There's still something else for me to do."

Sanford

For Sanford E. Gaylord, being photographed for the drug guide cover was a continuation of his journey with HIV.

"I remember that very fondly because I worked at Test Positive Aware Network [later known as TPAN, former publisher of POSITIVELY AWARE]," he says. "I had gone from attending support groups to being a volunteer to working at the organization. I was actually quite humbled and excited to be asked to be in it. It came at a time

COURTESY OF SYLVIA O'SHAUGHNESSY

when I was in the greatest amount of fear about living with HIV—*who would touch me, who would love me, who would even want to be around me if they knew I was living with HIV*? For me to literally come out of that closet, as well as coming out of the gay closet, I came out of them both at the same time. It was empowering because I no longer had to live in fear. I was able to do what others had done for me. They showed that you can live and thrive with HIV. This was my way of paying it forward. It would be a great opportunity for folks to see other folks of color, particularly those of African descent."

Like O'Shaughnessy and many other people diagnosed in the '80s and '90s, Gaylord was told he did not have much time. "We were preparing for our deaths," he says. "I was living out my dream. I was going to college thinking I wouldn't get my degree before I die. I was told to get my affairs in order, that I wouldn't live to be 30. I was 32 at that time, and was waiting to die. That's when things slowly started to change."

He pointedly remarks that he has outlived the doctor who had given him his initial grim prognosis. Gaylord has gone on to pursue careers in writing and acting, receiving recognition for his work. "I wrote many articles for the LGBT press, becoming an award-winning writer writing about being a Black gay man living with HIV in 1998," he says. "I've had the opportunity to appear in three documentaries and three films. I've worked from community-based organizations to the United States Department of Health and Human Services. It's been an incredible journey."

Still, surviving amidst the loss of so many friends and loved ones has left him with mixed emotions. "To still be here dancing upon the earth instead of lying under it, I feel beyond privileged and blessed to still be here," he says. "I still have an enormous amount of guilt that I feel because I'm still here. I'm still triggered because we just went through COVID, which unearthed things that I had compartmentalized.

"I think that it's just become more manageable, to be bluntly honest," he admits. "I have learned to make new friends. I have learned to create chosen family. I didn't think that I'd be able to do that 26 years ago when I lost my best friends, one to cytomegalovirus, another one had PCP [pneumonia] and then TB. Imagine losing the people who are your rock when you've already been disowned by your family because you chose to acknowledge that yes, *I am*. I had so many losses that I started to compartmentalize and didn't make new friends. I can make friends now. It's not easy, but I'm managing it better. I know that because I'm here, I'm charged with telling my story."

Asked what he would tell his younger self from the photo shoot 27 years ago, Gaylord pauses then says, "Stay curious, ask questions. There isn't much I can tell my younger self; I just needed to fucking *learn*. I had too much mouth. Way too much mouth. I would say, *be quiet a bit more and listen*. Process a little bit more. You are not a biohazard. Allow yourself to be loved. There is life after diagnosis. If you claim it."

COURTESY OF SANFORD GAYLORD · CHHOEUN: ENID VÁZQUEZ

Interactions and intricacies

A pharmacy student gains an appreciation for HIV treatment

Justin Chhoeun, a second-year pharmacy student at the University of Illinois at Chicago (UIC), was born the year POSITIVELY AWARE's annual HIV drug guide was first published. Pharmacists can play an important role in a person's health, he says, which is one reason why he's interested to learn about HIV treatment.
—**RICK GUASCO**

What got you interested in specializing in HIV?
I became interested in HIV after being on rotation at the infectious disease clinic at UIC. My pharmacist preceptor (Rodrigo Burgos, PharmD, AAHIVP) specialized in HIV and made an originally difficult topic easier to understand. After working with him for the semester and seeing the impact and connections he made with his patients, I slowly gained an appreciation for the work that goes into caring for this patient population. Although I did love patient interactions, understanding the intricacies of treatment regimens was definitely a huge player in why I am so interested in HIV.

Is there anything about HIV or HIV treatment that you didn't know about that surprised you?
One of the things that most surprised me about HIV treatment was how far we have come. First-line treatment is one pill a day compared to the regimens in the past. Even if patients develop resistance, there are still so many drugs up our sleeves that we can still get patients to live normal lives. Growing up as a gay man, I had always thought HIV diagnosis would be a death sentence but it just really is not the case anymore with today's innovations. It is one of my favorite things I learned about HIV!

What are some of the key issues or factors you are discovering as you're studying?
One research question I discussed with my preceptor was how to determine the value of pharmacist interventions in an HIV clinic. Although I am biased and can see the direct impact my pharmacist makes on patients' lives, how can we quantify these interventions so that institutions and clinics can also see this value? Not only does it answer the question of "what is the value of a pharmacist in this setting?" but also it paves a path to mobilizing more support for patients living with HIV.

What do you see as your role in the life of a person living with HIV or within the healthcare system?
It's hard to say what I want my role to be when it comes to HIV, but I do know that increasing patient access to medications has been one of my long-running thoughts. There is a population that cannot afford the medications needed to treat this condition and I wish there was more I could do as a future pharmacist to change this.

BEING BRIDGETTE
Bridgette Picou

‘Those conversations’

Talking about the ‘D’ word—*disclosure*

Once I have a desire to say something, in general I say it. I can temper my thoughts and tongue in situations where I think it makes sense to do so, but I like and believe in the power of open conversation for avoiding misunderstandings.

The value of open conversation increased for me as I learned to live with my HIV status. You know, because of the “D” word. No, not *that* one, the *other* one. *Disclosure.* Disclosing status should be an open conversation. It gets easier, but I don’t know if it ever evolves to being simple. Too many layers to consider. Who, when, how much to say, and it’s rarely the same twice because everyone is different.

I don’t know how your disclosure story is evolving. For me as a cisgender woman, in many ways it has given a small sense of empowerment. Strange concept, right? HIV giving a sense of power? I’ve gone from not being able to imagine telling anyone and writing sex off completely, to being able to be matter of fact about it, but also keep it a personal conversation. I don’t feel the need to convince anyone of who I am or beg for affection or for someone to date me. I’m better able to negotiate the conversation and the sex.

Negotiating sex or negotiating intimacy is a name for a concept folks do all the time that I had never heard of until sometime in my adulthood. (It is not about payment for sex.) It’s often that we take for granted situations, or don’t even know a thing is a “thing” until science or psychology or the medical establishment puts a name to it. In a general nutshell, *Negotiating Sex* is the idea of having conversations about sex before the sex to maximize pleasure, minimize danger, discuss limits and desires, and may *(should!)* include sexual health discussions. It equalizes the right to say no, the balance of power and the ability to control your sex life. I’m not leaving men out of this conversation. While traditionally, men wield the power in sex dynamics, if you are same sex loving or live outside of cis/hetero traditional partnerships, this concept rings true for you as well! While it is something we should and can do as people, many, like me, have never heard of it, or if we have heard of it, feel powerless to put into practice.

Having to do the big “D” takes an amount of courage. The stigma surrounding HIV makes most people feel like it is the worst thing in the world. For me personally, it’s not. Having to disclose and, in essence, lay myself bare, gives me the boost I need to ask the hard questions in return. I don’t know if it’s the shock of my disclosing I’m living with HIV, or just that I have the nerve to be living my life out loud, but men seem to really struggle when I turn the question back on them.

Do you know your HIV status? When was the last time you were tested, if ever? Do you have a history of other STDs? What does sex look like for you? The discomfort I can see in their body language and on their faces. The hemming and hawing of trying to make excuses about testing. The transfer of whose responsibility it is to do so. For the record, having someone else tell you their sexual history and that they are STI (sexually transmitted infection) free, does not excuse you from getting tested yourself nor mean you are necessarily STI free.

Perhaps it’s just the mental shift of having to go from judging my positivity (pun intended), to having to judge and examine their own sexual history and choices in the same conversation that gives them pause. Like, how dare I question them when I have this disease, right? I’m “supposed” to be grateful they are even considering having sex with me.

Let me encourage you, outside of disclosure, to make it a practice to negotiate sex. To find the balance in your needs and desires vs. your partner’s. You should ensure the sexual health of your body regardless of HIV status through open communication. To ask the hard questions in the short term is to get the comfort of knowing in the long run.

Be well. You matter.

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 the president-elect of the Greater Palm Springs Chapter of 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.

PICOU: CHAD SAIN · ILLUSTTRATION: ISTOCK