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HONORING **THIRTY YEARS** PUBLISHED BY TPAN
MARCH+APRIL 2020

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DHHS recommendations for first-time therapy

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A sneak peak at new drugs coming soon

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HIV medications and weight gain

THE 2020
HIV DRUG GUIDE

POSITIVELY AWARE

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EDITOR-IN-CHIEF
JEFF BERRY
@PAeditor

ASSOCIATE EDITOR
ENID VÁZQUEZ
@enidvazquezpa

HEPATITIS C EDITOR
ANDREW REYNOLDS
@AndrewKnowsHepC

CREATIVE DIRECTOR
RICK GUASCO
@rickguasco

PROOFREADER
JASON LANCASTER

PHOTOGRAPHERS
JOHN GRESS
CHRIS KNIGHT

ADVERTISING MANAGER
LORRAINE HAYES
L.Hayes@tpan.com

DISTRIBUTION MANAGER
DENISE CROUCH
distribution@tpan.com

SUBSCRIBE OR ORDER COPIES
positivelyaware.com/subscribe

LIVE LIFE POSITIVELY AWARE.

FOR 30 YEARS, PUBLISHED BY
TPAN
5537 N. BROADWAY
CHICAGO, IL 60640-1405
(773) 989-9400
FAX: (773) 989-9494
inbox@tpan.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.

COMFORT FOOD: Roy Ferguson, Mike Winkfield. Danielle Kruse, Frankie Franklin-Fox, Chancelor Cuningham, Chad T. Hendry, Anthony Johnson, and Quintin bonding at Nookies restaurant.

Among friends

BY **RICK GUASCO**

SHARING A MEAL can be such a communal experience. A gathering of friends, acquaintances, or even strangers who come together for one purpose. We find comfort and kinship in each other. That was the idea behind the cover of this year's HIV Drug Guide. The eight people who took part in the shoot found common ground and quickly took to each other, sharing their life stories.

"After my partner makes breakfast, I eat and take my HIV medication," said **Mike Winkfield**, who has been living with HIV for 18 years.

"I take my HIV meds daily and am undetectable," says Winkfield's partner, 68-year-old **Roy Ferguson**, who has been living with HIV for 23 years. "After being down-sized out of my job at 55, I turned to become an HIV/AIDS advocate. I work with fellow military veterans who are HIV-positive, coordinating a self-help/education group at Hines VA hospital."

"When I was diagnosed 10 years ago, I was scared that I would never be normal," said **Chad T. Hendry**. "Today I know better. Taking my pill every night consistently gives me the assurance that I am undetectable, and that I can't transmit to my partner. I am not bound or held back by fear of transmitting to someone I care about. That is a huge freedom."

Anthony and **Quintin** are a magnetic couple; Anthony is on PrEP and Quintin has been living with HIV for three years.

"HIV required me to get in front of my overall health," Quintin said. "Through organizations, peer navigators, and health professionals I was able to address my barriers to health self-sufficiency in two years. Taking charge of my health and wellness and taking my HIV medication helped me to get to undetectable. Learning to read my own labs and learning how to build trust with my health care providers gave me the peace of mind to keep striving. Making sure my partner remains negative also takes priority as part of my journey of living with HIV."

"I have been on PrEP since 2014, and I wholeheartedly believe that if taken correctly, it can be an effective tool for addressing HIV," Anthony said. "PrEP has played an important role in my relationship and provided me the opportunity to really be in love with someone living with HIV. It has helped me to navigate what being in a magnetic relationship looks like not only for myself but my community as well."

"Since I was diagnosed in 2016 with a T cell count of 10, I have been adherent with my HIV medication, said **Danielle Kruse**. "I have my own business, and am constantly on the move. But regardless of my day or night, my HIV med is always my nightcap. My T cells are now over 500, my business is growing, and I feel good."

"It has become second nature to take my meds," said **Frankie Franklin-Fox**, who acquired HIV through a blood transfusion 39 years ago. "After all these years, starting with AZT in 1995, it has become quite simple. I set the alarm on my phone so that I'm on time, and my meds are about 12 hours apart. Currently, the only side effect I experience is severe hair loss. But it's only hair! My viral load was 155,000, and I am now undetectable!"

"I was diagnosed with AIDS 30 years ago," said **Chancelor ("Chance") Cunningham**. My doctor had me on 15 pills a day. Today, I'm undetectable and take only one pill a day."

Nookies, a neighborhood restaurant near TPAN (the non-profit HIV/AIDS services organization that publishes POSITIVELY AWARE), generously served as the location for the photo shoot. It's where I often meet a friend for Sunday breakfast and take my HIV medication. As creative director, I was inspired by this for the cover, which was photographed by **John Gress** and styled by **Wyll Knight**.

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The 24th Annual HIV Drug Guide

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THE **PHARMACIST**

Eric K. Farmer, PharmD, BCPS, AAHIVP is an HIV clinical pharmacist at the Indiana University Health LifeCare Clinic at Methodist Hospital in Indianapolis, one of the largest providers of HIV medical services in the state of Indiana. He was instrumental in starting formal clinical pharmacy services there in 2009. He provides pharmacy services that include medication adherence counseling and patient education, drug information services, medication procurement, medication therapy management, and medical care coordination services. He is on the Board of Directors for the American Academy of HIV Medicine and serves as clinical faculty for the Midwest AIDS Training and Education Center. Dr. Farmer graduated from Butler University with his Doctor of Pharmacy in 2007. He then completed an ASHP-accredited PGY1 pharmacy residency at Eskenazi Health (formerly Wishard Health Services) 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**

Ross A. Slotten, MD, MPH, is a family physician who has treated people with HIV/AIDS since 1982. Dr. Slotten graduated from Northwestern University School of Medicine in 1981, completed his training in family medicine at St. Joseph Hospital in Chicago in 1984, and received a master's degree in public health from the University of Illinois in 1992. He has cared for more than 1,000 people with HIV, has participated in numerous studies related to HIV/AIDS, and remains in active clinical practice. He is currently affiliated with the Amita Health Group/St Joseph Hospital in Chicago. He is the author of the upcoming memoir, *Plague Years: A Doctor's Journey through the AIDS Crisis*, to be published by the University of Chicago Press this spring.

THE **ACTIVIST**

Bridgette Picou has played a mix of roles along her life's journey. Currently working as a licensed vocational nurse at Desert AIDS Project in Palm Springs, California, she is also an active HIV blogger, contributor to the CDC's "Treatment Works" public service campaign, and is working towards several HIV ambassadorships. She is a mom, grandmother, friend, and nurse, each piece a part of the whole picture. Diagnosed with HIV at almost 40, she re-examined her life and found a new path, which is where nursing came in. It may have taken a while, but she believes nursing is what she was always meant to do. Working in the HIV field has given her a dual perspective on HIV, seeing it from both the patient's and the provider's standpoint. Whether providing balance, or as a light to those struggling at diagnosis, navigating survival is her motivation. Finding a voice in advocacy and activism is a natural progression, since she feels that every time she fights for someone else, she affirms her own life.

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 a much condition fueled by societal discrimination as it is by a virus. As such, it makes her reporting socio-political as well as medical. She enjoys reporting on medical updates and making them relatable to readers' lives. Enid has a special interest in sexual violence and sexual freedom, and in serving the sex trade worker and transgender communities.

THE **EDUCATOR**

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

FARMER AND VÁZQUEZ: JOHN GRESS • SLOTTEN: ERIC HERZOG • BLIEDEN: ISAAC MORA

EDITOR'S NOTE

JEFF BERRY

Reasons for hope

In this day and age it's easy to find reason to despair. But when it comes to HIV treatment and drug development, there are many things that continue to give us hope.

This is the 24th annual POSITIVELY AWARE HIV Drug Guide, which provides invaluable information on HIV treatment and care. The HIV Drug Guide is used as a resource throughout the year by people living with HIV (PLHIV) and their providers, and is our most requested issue every year. As I sat down to write this note, I went back to the 2007 Drug Guide to see what's changed—and what has remained the same.

Back then I wrote:

2007—not only did many of us think we would never live to see it, but the fact that there are now nearly 30 drugs for us to choose from to construct an anti-HIV regimen is almost unfathomable. Yet here we are.

We have much to be thankful for. Many new therapies are in the pipeline, and at least three are nearing approval. One is already in expanded access, another is due to open in the next few months, and both of these are in entirely new classes of drugs. It's being said that we will probably never again be in such good shape as far as new drugs and opportunities to combine them, at least not in the near future.

Yet here it is 13 years later, and we are in good shape once more! Today we list 39 HIV drugs in the guide, and if you add in all the drugs currently on the market including those that are seldom or rarely used, there are actually 50 drugs. Some of the more recently approved drugs (such as Cimduo or Temixys) are what in the past we would have called "me too" drugs, although that phrase has taken on a whole new meaning in the last few years. With the continued introduction of generics and "quasi-generics" (co-formulations with one or more generic drugs as a component) these "look-alike" drugs serve a purpose by potentially keeping the price of the drug lower, and copays fewer.

This year, as in 2007, we have exciting new drugs in the pipeline (see page 63), including for people who are heavily treatment-experienced and have multi-drug resistance, such as fostemsavir, and leronlimab. As people live longer with HIV but have run out of options, it's good to see medications being developed for this population. The investigational cabotegravir/rilprivirine LA will soon offer a completely new choice for HIV therapy, a monthly injection that is a complete regimen all in one.

Weight gain is an increasing concern for those on antiretroviral therapy (ART), so Dr. David Wohl (see page 8) looks at the evidence we have to date, what steps you can take now, and things you may want to consider for the future.

We had people dying in 2007 while being placed on waiting lists for state AIDS Drug Assistance Programs (ADAPs). While those waiting lists are gone, they've been replaced by the continued assaults by this administration on vulnerable populations and on the Affordable Care Act (Obamacare), the rising prices of pharmaceutical drugs, and soaring healthcare costs including premiums, cost-sharing, and deductibles, that are unsustainable. In January, the administration issued guidance that allows states to request capped block grant funding for their Medicaid programs. Medicaid accounts for 30% of all federal spending on HIV care (second only to Medicare), and provides coverage to 42% of PLHIV, says NASTAD's Dori Molozanov in a recent blog. "A block grant would lead to cuts in access to services with negative consequences for vulnerable populations, including people living with or at risk for HIV and hepatitis, who depend on Medicaid coverage in order to receive the care they need."

On the plus side, what we didn't know then but do now is that PLHIV on treatment who have an undetectable viral load cannot sexually transmit the virus (U=U, or undetectable equals untransmittable). But making sure people have universal access to HIV medication (the third U) is crucial, and we also need to ensure that we continue to support and aren't stigmatizing those who for whatever reason cannot achieve or maintain an undetectable viral load.

This drug guide would not be possible without a team of experts who make all the magic happen. A heartfelt thanks to Dr. Ross Slotten (my fabulous personal physician), Bridgette Picou, Dr. Eric Farmer, Dr. Carla Blieden, Dr. David Wohl, Enid Vázquez, Rick Guasco, Jason Lancaster, Andrew Reynolds, John Gress, and Wyll Knight.

Let's keep looking for reasons to hope, because they are still here. It may just be that we have to dig a little bit deeper to find them.

Take care of yourself, and each other.

While those ADAP waiting lists are gone, they've been replaced by the continued assaults by this administration on vulnerable populations and on the Affordable Care Act (Obamacare), the rising prices of pharmaceutical drugs, and soaring healthcare costs including premiums, cost-sharing, and deductibles, that are unsustainable.

WEIGHTY CONCERNS

What we know for now about weight gain with HIV medications

BY DAVID ALAIN WOHL, MD

A long time ago, I was in sitting in a sunny office at work getting scolded by a couple of guys from a drug company. The previous week, at a conference presentation in New York I had told the large audience of HIV doctors to take their patients off the antiretroviral that these guys sell since it was clear that it melted the fat tissue—perhaps in a reverse order of importance—of the arms, legs, butt, and face, causing irreversible disfigurement. These two did not like that, not one bit.

"Do you realize, doctor, the harm you could cause by urging clinicians to hastily change HIV meds?" When I cited recent reports and my own observations, one, a doctor himself, chided that I know (or should know) that association is not the same as causation. Regretfully, I did not tell the pair to fuck off, but stick tight to my guns I did, saying that: a) their drug is toxic, b) they know it, *and* c) I would continue to tell people to avoid prescribing it (which, I guess, is basically the same as telling them to fuck off).

A rerun of that meeting plays most times I see the hollowed cheeks of the veterans of those early days of highly active HIV therapy; I ask myself if I recognized soon enough the effects of the "d" drugs—d4T and ddI? Could I have protected more people from their ravages? Such an experience sensitizes you and that makes you less likely to miss the opportunity to act early the next time. So, recently as murmurs grew to a roaring alarm that newer HIV medications may be messing with fat—not melting it but laying it on thick—I thought about the meeting with the drug company dudes, the abandonment of the d-drugs soon after, and a foreboding that here we go again.

WEIGHT GAIN AND HIV THERAPY

Weight is tricky. People are either trying to lose it or gain it (okay, mostly lose it in super-size-me America) with hardly anyone who isn't incredibly annoying saying they are at the perfect weight and absolutely happy with where the scale's needle lands. HIV makes this even trickier. Big-time weight loss can happen in those with more advanced disease and is a tell-tale sign of basement-level CD4 cell counts, but nowadays most people don't come into care that far along. Rather, like most of their HIV-negative compatriots, those who are newly diagnosed with HIV are often overweight—even if they are down a few pounds from their normal. Once they start HIV meds, the pounds come back—a good sign that the meds are working.

However, not all weight gain is created equal or welcome. Starting a year or two ago, some clinicians observed that people starting on regimens that include antiretrovirals in the integrase inhibitor class experience weight gains exceeding those seen in people treated with regimens not containing this drug class. Soon thereafter, the differential effects of antiretrovirals on weight were looked at in larger and larger

PKLINE /ISTOCKPHOTO

STARTING A YEAR OR TWO AGO, some clinicians observed that people starting on regimens that include antiretrovirals in the integrase inhibitor class experience weight gains exceeding those seen in people treated with regimens not containing this drug class.

datasets of people living with HIV, including those starting HIV therapy and those switching from one type of regimen to another. Pretty consistently, the integrase inhibitors, especially the two newest, dolutegravir (DTG) and bictegravir (BIC), were being linked independently to relatively greater gains in weight.

A crescendo of clinical trial data this past year has further moved this from speculation to major concern to fact. Of these, three tell us most of what we now know: the ADVANCE trial, an analysis of Gilead trial data, and the DISCOVER trial.

THE ADVANCE TRIAL

The objective of this study was not to look at changes in weight but to compare more modern HIV regimens with older, standard treatment used in South Africa, where the study was conducted. Over 1,050 people were randomized to start HIV therapy with one of three regimens:

- tenofovir disoproxil fumarate (TDF)/ emtricitabine (FTC)/ efavirenz (EFV) [Atripla]
- TDF/FTC + DTG [Truvada + Tivicay]
- tenofovir alafenamide fumarate (TAF)/FTC + DTG [Descovy + Tivicay]

Approximately 60% of those enrolled were women, and when entering the study about half of all the participants had a body mass index at or above the threshold indicating being overweight. Overall, each of the regimens did a good job of getting the viral load suppressed and were well-tolerated, with some trends favoring the DTG arms. However, it was noticed that there were significant differences in the amount of weight people gained after starting these regimens.

Those treated with DTG gained much more weight than those treated with TDF/FTC/EFV, and these gains were even greater with the use of TAF with DTG. Plus, women experienced greater increases in weight than the men regardless of what regimen they were assigned.

Notably, weight did not plateau during the study but continued to increase over time. Also, based on body composition analyses done on a subset of participants, the accumulated weight seemed due to increases not just in trunk and limb fat, but also lean (non-fat) tissue.

The factors associated with weight gain of 10% or more during the study included not just being assigned TAF and/or DTG but also being a woman, having low CD4 cell count, a high viral load, or a higher weight at baseline.

This study shows very clearly how different regimens impact weight, with DTG leading to greater gains, an effect that is exacerbated with concomitant use of TAF, and that women are more likely to be affected than men.

This trial was done in South Africa among people from that country and neighboring Zimbabwe. However, analyses of data collected from those living in the U.S. have found similar medication, race, and gender associations with excessive weight gain while on integrase inhibitors.

GILEAD TRIALS ANALYSIS

While the weight gain buzz is swarming mostly around DTG (dolutegravir), there has been little more than speculation available about whether or not its integrase sibling, BIC (bictegravir), has the same impact on weight. Gilead Sciences, the maker of BIC, TDF, TAF, and elvitegravir (EVG, an older integrase inhibitor found in Genvoya and Stribild), reported in the journal *Clinical Infectious Diseases* an analysis of weight changes measured during eight of their large clinical trials of initial HIV treatment, including, collectively, over 5,000 participants (90% male, 26% Black). These hark back to the 934 trial in which AZT/3TC [Combivir] and EFV [Sustiva] was compared to TDF/FTC/EFV, as well as later studies involving atazanavir and rilpivirine (RPV), and more recent comparisons involving BIC, DTG, and TAF.

In addition to factors expected to predict gains in weight, such as low CD4 cell count, higher viral load, and not injecting drugs, as well as the risk of being female and being Black seen in other studies, there were significant treatment-associated effects observed. Once again, integrase inhibitors were associated with the biggest jumps in weight after the start of therapy with both BIC and DTG having the largest and indistinguishable effects. As was seen in the ADVANCE trial, those treated with TAF became heavier than those receiving TDF or abacavir (ABC).

This analysis helps to outline a hierarchy of weight gain risk with DTG and BIC being very similar and higher than elvitegravir (and likely raltegravir, or Isentress). Among the nucleosides, TAF has a greater effect than TDF and ABC. For the non-nucleosides, a modestly bigger change in weight was seen with RPV compared to EFV. The only protease inhibitor studied was atazanavir (Reyataz), and it behaved a lot like the non-nucleosides.

THE DISCOVER TRIAL

All studies, as well as clinical experience, show us that many people starting HIV therapy gain some weight. For some, weight gain is seen to be a consequence of getting healthier, the so-called "return-to-health" phenomenon. As the virus becomes controlled, the idea is that energy is saved and stored as fat. Appetite can also increase as the immune system starts to normalize. Such a phenomenon can be seen in the ADVANCE trial and the Gilead studies where those who entered with indicators of more advanced HIV disease gained more weight than those whose numbers were healthier. This can make it difficult to know if it is a medication itself that is causing the packing on of pounds or its intended (beneficial) antiretroviral effects. By studying those whose virus is well-controlled and who switch their HIV meds we can get around return-to-health issues, but this may not fully answer the question of whether a drug or regimen inherently increases weight. For example, switching from EFV, which is taken on an empty stomach before bed, to a regimen without food restrictions may lead to gains in weight simply because of the more liberal food allowance. The same sort of thing can happen if a regimen that causes some low-level gastrointestinal problems, such as a boosted protease inhibitor, is swapped out for one that is free from such issues. To get around this confounding, we can look at studies done in people who don't have HIV, like PrEP trials.

The DISCOVER trial compared TDF/FTC (Truvada) with TAF/FTC (Descovy) as PrEP for over 5,000 men and trans women. After 96 weeks, the median gain in weight among those assigned TAF/FTC was about four pounds, compared to one pound in those on TDF/FTC. So, in this PrEP trial, in which return-to-health is not an issue, the differential effects of TAF versus TDF is made clear. Even so, this does not necessarily mean TAF causes weight gain as it could be TDF suppresses weight, or it could be some of both. But, to the person on the scale or trying on new jeans, this is beside the point. >>

WEIGHT CHANGES

Baseline to Week 96 during the ADVANCE trial (IN POUNDS)

	TAF/FTC + DTG	TDF/FTC + DTG	TDF/FTC/EFV
WOMEN	20	11	7
MEN	13	7	2

>> WHAT YOU SHOULD—AND SHOULD NOT—DO

At this point, you may be cursing your HIV meds (and your HIV doc) for making you fat. But it is really important to understand that weight is complicated and influenced by many physical, psychological, and even environmental forces. For many people who are unhappy with their weight and are on the very HIV meds that have the strongest association with tipping the scales, the drugs might not be the issue at all. It is incredibly helpful to look at trends, particularly for any change in weight that corresponds to the initiation or change in HIV therapy.

Someone whose weight has hovered between 250 and 260 pounds before *and* after switching their regimen from TDF/FTC/EFV (Atripla) to TAF/FTC plus DTG (Descovy plus Tivicay) cannot pin blame on the new meds. In contrast, a jump in weight that occurred soon after starting TAF/FTC/BIC (Biktarvy) without any major changes to diet, exercise, or other medications would squarely implicate this regimen as the cause.

What to do in such cases where the smoking gun leads to the HIV regimen? This, sad to say, is still unclear as there are no data to rely on for guidance. We know that excess weight can be a serious threat to health and has been associated with diabetes, hypertension, fatty liver, sleep apnea, and wear and tear of the joints, among other problems. In addition, weight gain can be a serious hit to a positive body image. Therefore, this is not something to simply tolerate.

In clinical trials, the new non-nucleoside doravirine (Pifeltro) combined with TDF/FTC (Truvada) or ABC/3TC (Epzicom) has been found to produce small changes in weight among those starting HIV therapy that are on par with those seen in the study participants treated with these nucleosides and EFV or darunavir/ritonavir (Prezista/Norvir). Whether switching to doravirine from DTG or BIC reverses weight gains is of interest but has not yet been studied, although it would be reasonable to assume it might. Also, whether cutting calories or carbs and/or exercising more can beat back excessive fat despite the continuation of the offending HIV med is not clear—but there are compelling benefits of these lifestyle changes, and so they are recommended, regardless.

Some may ask whether we should continue to use the HIV meds that are linked to greater weight gain, given the health and body image risks. Is not excessive weight gain the lipodystrophy of our time? These are valid questions and if we learned anything from the d-drug debacle it is to never be complacent.

However, there are several ways in which, at least right now, this is not a replay of d4T and lipoatrophy. Foremost, the newer integrase inhibitors are otherwise really, really good medications. They are potent, have minimal other side effects, play well with other medications, and have a super-high barrier to resistance. The recent pushback by many women living with HIV against any blanket limitations to DTG use following initial concerns about an association with birth defects is telling and speaks to the benefits of these newer meds.

TAF's advantages over TDF are also pretty clear—just ask all those critical that it was not made commercially available sooner.

Further, it seems that a lot of people do not experience major weight gains on these meds. In the ADVANCE trial, around half of the women and close to 70% of the men in the TAF/FTC + DTG group had minimal change or even a decrease in weight after 96 weeks—and, as mentioned, some of this weight gain was probably influenced by factors such as advanced HIV disease and simply starting on HIV therapy.

Still, more data will reveal the depth of the problem and if the risk-to-benefit analysis changes.

People who think HIV meds could be responsible for an increase in weight should discuss this concern with their clinician. A look at the records can tell if any changes in HIV therapy correspond to changes in weight.

It is important to also look for other causes, such as starting a new depression medication or stopping smoking at around the same time, or changes in activity levels or eating habits that could confuse the picture.

When starting initial HIV treatment, it is critical that clinicians warn patients about the potential effects of certain meds on weight and then monitor weight over time. Again, given their overall advantages over older drugs, the newer antiretrovirals continue to make sense to use in most cases. However, for those at highest risk of excessive weight gain, such as a Black woman who is obese and trying to shed pounds, avoiding BIC, DTG, and TAF may be justified. It is absolutely essential that all such decision-making be shared between the clinician and the patient.

CONCLUSIONS

There is clear evidence that newer HIV medications including DTG, BIC, and TAF can cause greater increases in weight than other antiretrovirals and that women, especially women of color, are at higher risk than men for experiencing greater gains in weight on therapy. The mechanism explaining the differential effects of HIV medications on weight remains unclear and is likely to be complicated. People living with HIV and their providers should track weight carefully and look for unexpected or unexplained changes to determine if antiretroviral therapy could be the cause. More research is planned to understand if switching from suspect HIV medications to those that have not been associated with excessive weight gain can lead to a drop in weight. Until these studies provide guidance, practical interventions including the adoption of a healthful, plant-based, diet and regular exercise should be attempted along with informed switches in HIV therapy based on the data that are available. PA

DAVID ALAIN WOHL, MD is a professor of medicine at the University of North Carolina at Chapel Hill. There he leads the HIV Prevention and Treatment Clinical Research Site and sees patients in the university's Infectious Diseases Clinic.

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THE WAXING AND WANING OF HIV DRUGS

Medications come and go, but the goal is still the same

BY **ROSS A. SLOTTEN, MD**

For those of us who have been treating people with HIV/AIDS since the earliest days of the epidemic, 2020 is a completely different world. Today, we take for granted that nearly everyone with HIV who comes into our care not only can be successfully treated with an array of life-saving medications but is also likely to live a normal lifespan, unless diabetes, cancer, heart disease, or some other illness cuts their lives short. If they adhere to their medication regimens, people living with HIV will not die of AIDS. With several dozen anti-retroviral agents at our disposal (and more in the pipeline), you almost have to go out of your way to fail treatment and die of an AIDS-related problem.

Of course, there still exist areas in the United States where people living with HIV do not have easy access to treatment. And those at highest risk, especially young LGBT men of color, often don't perceive of themselves as being at risk or may not know much about HIV and other sexually transmitted diseases. Unless as a society we address issues of inequality and bring the marginalized into the mainstream, the epidemic will continue to rage, even though the epidemic could, in theory, burn out in a generation or two with universal treatment of those with HIV and universal prevention in those at risk. With no vaccine or cure in sight, that is our best hope.

In this issue, I would like to focus on the highly active anti-retroviral treatments (or HAART) that most experts prefer to prescribe. For the most part, I agree with the Department of Health and Human Services guidelines for the use of antiretroviral agents in adults and adolescents with HIV. The top-tier agents have been given an A1 rating, "A" standing for strongly recommended by an expert panel and "1" for having undergone one or more randomized trials with positive clinical outcomes and/or validated laboratory end points (undetectable viral loads, for example). Those rated "B" are moderately recommended and those rated "C" are recommended only under certain circumstances.

In reality, many different regimens will work beautifully. Crixivan, AZT, and 3TC are just as effective as Biktarvy and saved many lives, but no one in this era would prescribe Crixivan, AZT, and 3TC because of pill burden, inconvenience, and unacceptable long-term side effects such as disfiguring lipodystrophy.

I have elected not to comment on Complera and Stribild this year because they have been replaced by Odefsey and Genvoya, respectively, which are essentially the same but have better safety profiles than their progenitors. I've also omitted Epivir (3TC), Emtriva (FTC), Ziagen (abacavir), Edurant (rilpivirine), and Viread (TDF) because of redundancy (they are components of other regimens). I have written about some of the so-called generic medications, such as Cimduo and Symfi, not because I believe in them, but because they are marketed as less expensive alternatives to the top-tier agents.

The issue of cost is important and complicated. How are HIV medications priced and why? All HIV medications are expensive, whether the price is $1,500 per month or $3,000 per month. Those costs are average wholesale costs. Only people without insurance would actually pay full price. Don't feel sorry for your insurance company and don't believe a word about "true costs" from the pharmaceutical industry. The relationship between the insurance and pharmaceutical industries is complex, unfathomable, inscrutable, opaque—in short, anything but transparent. These two devils play a game that excludes, but nevertheless ensnares, most of us.

The current paradigm of HIV treatment is a nucleoside backbone (TDF/FTC; TDF/3TC; TAF/FTC; or ABC/3TC) plus an integrase strand transfer inhibitor (INSTI) or boosted protease inhibitor (PI). That paradigm may shift. Two-drug combinations, including those without nucleosides, show promise in some patients who have never been treated before. Crixivan and Kaletra, once kings in the HIV-treatment world, are now nearly forgotten. In 10 years, Biktarvy and Triumeq may have joined them as newer treatments replace them. HIV drugs, and HIV drug combinations, come and go, which is why this HIV drug guide remains necessary and useful. PA

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Getting the most out of your drug guide

Below are tips to help you and your care providers make empowered, informed treatment decisions. Medications included in the 2020 HIV Drug Guide are those most commonly used, or expected to be approved in the coming year.

With so many choices out there, we order the drug pages by those that are the best options and list them first, followed by commonly prescribed drugs in each category. To quickly find your drug, go to the next page. On the pullout chart, drugs are listed by category and then alphabetically. Older drugs that are rarely used are only pictured (without dosing information) at the bottom of the pullout chart.

Goal of HIV therapy

Understanding HIV treatment is the key to success. The goal of therapy is to suppress the virus to an undetectable level (meaning the virus in your blood is so low, it cannot be detected by normal tests). This will keep you healthy, and the sooner you start therapy, the less damage to your immune system so you'll stay healthier, longer. When you are on effective antiretroviral treatment (ART) and undetectable (less than 200 copies) for at least six months, it also means you can't transmit HIV to your partner (undetectable equal untransmittable, or U=U). Getting to and staying undetectable means you need to take your medication as prescribed (for example, if it's with or without food), and not miss doses.

Drug names

When a drug is in development it's first given a "generic" or "scientific" name (such as dolutegravir). At medical conferences and in scientific publications you will often see three-character abbreviations used (DTG). Once it's approved, it's given its brand name (Tivicay), which most people know it by.

Drug classes, categories, and co-formulations

A fixed-dose combination (FDC) combines two or more drugs in one tablet, such as Prezcobix (darunavir/cobicistat). A single-tablet regimen (STR) is a complete regimen in one pill, such as Biktarvy (bictegravir/emtricitabine/tenofovir alafenamide).

Anti-HIV drugs should always be taken in combination using two or more drug classes (for example, an integrase inhibitor plus two nukes). Single-tablet regimens (STRs) are not a drug class but combine multiple classes of drugs into one tablet. STRs are widely used for first-time treatment and for their convenience, but they are not for everybody, including some people who are treatment-experienced or have multi-drug resistance.

Recommendations for use

The Department of Health and Human Services (DHHS) and the International AIDS Society-USA (IAS-USA) both publish recommendations for the use of HIV antiretroviral drugs. We include information on some of the recommendations on page 60, and at the top of each drug page, as well as in the pullout drug chart. DHHS and IAS-USA guidelines are very similar, but for consistency we reference the DHHS guidelines. For complete guideline recommendations go to aidsinfo.nih.gov or iasusa.org/resources/guidelines.

Drug pricing and access

The Average Wholesale Price (AWP) is listed on each drug page and is a way to compare costs of drugs. It is not what you would pay if you were to pay the full retail price. In the drug cost-sharing and patient assistance program charts (beginning on page 66) we include information on how to access programs that can help cover all or part of the costs of these medications.

Talking to your doctor

You can play an active role in your health care by talking to your doctor. Clear and honest communication between you and your physician can help you both make smart choices about your health. It's important to be honest and upfront about your symptoms even if you feel embarrassed or shy. Have an open dialogue with your doctor—ask questions to make sure you understand your diagnosis and treatment.

Here are a few tips that can help you talk to your doctor and make the most of your appointment:

- Write down a list of questions and concerns before your appointment.
- Consider bringing a close friend or family member with you.
- Take notes about what the doctor says, or ask a friend or family member to take notes for you.
- Learn how to access your medical records, so you can keep track of test results, diagnoses, treatments plans, and medications and prepare for your next appointment.
- Ask for the doctor's contact information and their preferred method of communication.
- Remember that nurses and pharmacists are also good sources of information.

More information online

Operated by the National Institutes of Health, AIDSinfo maintains factsheets on each HIV medication at aidsinfo.nih.gov/understanding-hiv-aids/fact-sheets/21/58/fda-approved-hiv-medicines. **DOWNLOAD** iPhone and Android apps that provide drug info, treatment guidelines, and a glossary: aidsinfo.nih.gov/apps. You can find the online version of your medication's drug page from our HIV Drug Guide by adding your drug's name after typing positivelyaware.com/ into your browser (for example, positivelyaware.com/*triumeq*). To see if your HIV drug interacts with another medication, both prescription and over-the-counter, **GO TO** hiv-druginteractions.org.

SKYNESHER -ISTOCKPHOTO

WHAT'S ON THE MENU?

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

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

PAGE	BRAND NAME	CATEGORY	GENERIC NAME
28	**Atripla**	STR	efavirenz/emtricitabine/tenofovir DF (EFV/FTC/TDF)
18	**Biktarvy**	STR	bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF)
41	**Cimduo**	NRTI*	lamivudine/tenofovir DF (3TC/TDF)
27	**Complera**	STR	rilpivirine/emtricitabine/tenofovir DF (RPV/FTC/TDF)
23	**Delstrigo**	STR	doravirine/lamivudine/tenofovir DF (DOR/3TC/TDF)
39	**Descovy**	NRTI*	emtricitabine/tenofovir alafenamide (FTC/TAF)
20	**Dovato**	STR	dolutegravir/lamivudine (DTG/3TC)
47	**Edurant**	NNRTI	rilpivirine (RPV)
43	**Emtriva**	NRTI	emtricitabine (FTC)
44	**Epivir**	NRTI	lamivudine (3TC)
42	**Epzicom**	NRTI*	abacavir/lamivudine (ABC/3TC)
35	**Evotaz**	PI/PKE	atazanavir/cobicistat (ATV/COBI)
24	**Genvoya**	STR	elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (EVG/COBI/FTC/TAF)
50	**Intelence**	NNRTI	etravirine (ETR)
32	**Isentress HD**	INSTI	raltegravir (RAL)
21	**Juluca**	STR	dolutegravir/rilpivirine (DTG/RPV)
37	**Norvir**	PKE	ritonavir (RTV)
26	**Odefsey**	STR	rilpivirine/emtricitabine/tenofovir alafenamide (RPV/FTC/TAF)
48	**Pifeltro**	NNRTI	doravirine (DOR)
33	**Prezcobix**	PI/PKE	darunavir/cobicistat (DRV/COBI)
34	**Prezista**	PI	darunavir (DRV)
36	**Reyataz**	PI	atazanavir sulfate (ATV)
51	**Selzentry**	EI	maraviroc (MVC)
25	**Stribild**	STR	elvitegravir/cobicistat/emtricitabine/tenofovir DF (EVG/COBI/FTC/TDF)
49	**Sustiva**	NNRTI	efavirenz (EFV)
29	**Symfi/Symfi Lo**	STR	efavirenz/lamivudine/tenofovir DF (EFV//3TC/TDF)
22	**Symtuza**	STR	darunavir/cobicistat/emtricitabine/tenofovir alafenamide (DRV/COBI/FTC/TAF)
41	**Temixys**	NRTI*	lamivudine/tenofovir DF (3TC/TDF)
31	**Tivicay**	INSTI	dolutegravir (DTG)
19	**Triumeq**	STR	dolutegravir/abacavir/lamivudine (DTG/ABC/3TC)
52	**Trogarzo**	EI	ibalizumab-uiyk (IBA)
40	**Truvada**	NRTI*	emtricitabine/tenofovir DF (FTC/TDF)
38	**Tybost**	PKE	cobicistat (COBI)
45	**Viread**	NRTI	tenofovir disoproxil fumarate (tenofovir DF, or TDF)
46	**Ziagen**	NRTI	abacavir sulfate (ABC)

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

HIV DRUGS EXPECTED TO BE APPROVED IN 2020

30	Brand name TBD	LA	cabotegravir/rilpivirine long-acting (CAB LA/RPV LA) injectable
53	Brand name TBD	AI	fostemsavir (FTR)
54	Brand name TBD	EI	leronlimab (PRO 140) long-acting injectable

HIV PREVENTION

58	**Descovy for PrEP**	PrEP	emtricitabine/tenofovir alafenamide (FTC/TAF)
59	**Truvada for PrEP**	PrEP	emtricitabine/tenofovir DF (FTC/TDF)

NON-HIV DRUGS

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

Biktarvy

BIC/FTC/TAF
bictegravir/emtricitabine/tenofovir alafenamide

STR SINGLE-TABLET REGIMEN CONTAINING AN INSTI AND TWO NRTIs

★ RECOMMENDED INITIAL REGIMEN FOR MOST PEOPLE

STANDARD DOSE

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

For adults and children weighing at least 55 pounds (25 kg) (youngest patients in research were 6 years old). Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. Biktarvy is not recommended for people with CrCl less than 30 mL/min or people with severe liver impairment.

- SEE ALSO DESCOVY, which is contained in this drug (bictegravir is not available separately).
- SEE PACKAGE INSERT for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

Most common side effects observed in study participants include nausea (5%), headache (5%), and diarrhea (6%). Six individuals in Study 1490 and none in Study 1489 stopped Biktarvy due to side effects, none of which were due to kidney problems. New data associate INSTIs and TAF with weight gain; see "Weighty Concerns," beginning on page 8, and GO TO aidsinfo.nih.gov. Serum creatinine, estimated creatinine clearance, urine glucose, and urine protein should be obtained before initiating Biktarvy and should be monitored during therapy. There have been rare reports of depression and suicidal ideation, primarily in patients with a history of psychiatric illnesses, in people receiving INSTI-based regimens. The DHHS guidelines recommend closely monitoring patients with pre-existing psychiatric conditions on an INSTI. Prior to initiation, people should be tested for hepatitis B (HBV) infection. Severe exacerbations of hepatitis B have been reported in people who are co-infected with hepatitis B and have discontinued the emtricitabine and/or tenofovir components. Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted.

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POTENTIAL DRUG INTERACTIONS

Do not take with rifampin or the anti-arrhythmic dofetilide. Not recommended to be taken with Epivir-HBV, Hepsera, or Vemlidy, all three for treatment of hepatitis B. Biktarvy can be taken at least two hours before or six hours after taking laxatives or antacids, the ulcer medication sucralfate, oral iron or calcium supplements (but these two can be used with Biktarvy if taken together with food), or buffered medications. Start metformin at lowest dose and titrate based on glycemic control. Monitor for metformin adverse effects. When starting or stopping Biktarvy in people on metformin, dose adjustment of metformin may be necessary to maintain optimal glycemic control. Not recommended with St. John's wort. Can be taken with the hepatitis C medications Epclusa, Harvoni, Sovaldi, and Vosevi. Not intended to be taken with other HIV medications, unless prescribed that way. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Received FDA approval in February 2018. For now, Biktarvy is a top dog in HIV treatment. See potential new side effect (weight gain). The data show that the bictegravir drug resistance barrier is comparable to that of dolutegravir and protease inhibitors (like Prezista). That is a huge advantage. Biktarvy is the first unboosted INSTI-containing STR with TAF, and one of four unboosted INSTI STRs overall (the others are Triumeq, Dovato, and Juluca). ("Unboosted" means that the primary antiretroviral drug, in this case bictegravir, does not require another medication such as Norvir or Tybost to increase its drug levels in the body.) This is a really big deal due to less drug interactions when there's no boosting. Biktarvy is a small INSTI-based STR tablet, which may help some individuals who have difficulty swallowing pills. Pediatric study is ongoing. At this time, there isn't sufficient data to support the use of Biktarvy during pregnancy.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$3,885.97/MONTH

DR. ROSS SLOTTEN SAYS: Biktarvy, a single-tablet regimen (STR) that contains the potent INSTI bictegravir and two nucleoside reverse transcriptase inhibitors (NRTIs), was approved by the FDA in February 2018. It is one of three A1 STRs recommended by the expert panel of the DHHS. Biktarvy has several virtues. Because bictegravir doesn't have to be boosted, there are very few drug-to-drug interactions. As people with HIV age, they may develop a number of medical problems, or co-morbidities, requiring treatments that often interact with a boosting agent like ritonavir or cobicistat. It also contains tenofovir alafenamide or TAF, which has less potential for kidney toxicity or loss of bone density, a potential problem for tenofovir disoproxil (TDF, brand name Viread). Moreover, it is very well tolerated and has few significant upfront side effects, like nausea, vomiting, and diarrhea. Because Biktarvy contains TAF and FTC, it can be prescribed for people co-infected with hepatitis B. Biktarvy is less fussy than some other HIV medications because it can be taken with or without food. Unlike Triumeq (see Triumeq page), which requires HLA-B*5701 testing to rule out hypersensitivity to abacavir, one of its three components, Biktarvy can be used as a first-line same-day ART regimen, if one chooses to initiate treatment on the day of diagnosis of HIV infection, regardless of viral load or CD4 count. To date, no integrase resistance to Biktarvy has been reported. Although Biktarvy is not necessarily better than other 3-drug regimens, its simplicity, safety, and tolerability make it an obvious choice as a first-line therapy.

ACTIVIST BRIDGETTE PICOU SAYS: A single-tablet regimen containing three medications, Biktarvy is a popular option for those newly diagnosed or those looking to simplify their current regimen. It is also an option for quick/rapid start initiation. An additional plus is it can be taken with or without food. As long as you are not resistant to any of the components it's worth a conversation with your healthcare provider. Side effects reported have been mild to moderate and usually clear within the first few weeks. Having said that, all side effects should be discussed with your healthcare provider, especially if severe (or even just annoying) enough for you to consider not taking your medication. Adherence matters for your long-term health.

Triumeq

DTG/ABC/3TC
dolutegravir/abacavir/lamivudine

STR SINGLE-TABLET REGIMEN CONTAINING AN INSTI AND TWO NRTIs

★ RECOMMENDED INITIAL REGIMEN FOR MOST PEOPLE IF HLA-B*5701 NEGATIVE

STANDARD DOSE

One tablet once daily, without regard to food, for people with no evidence of INSTI resistance. Tablet contains 50 mg of the INSTI dolutegravir plus 600 mg abacavir and 300 mg lamivudine. For adults and children weighing at least 88 pounds (40 kg). An additional 50 mg dose of dolutegravir (brand name Tivicay) separated by 12 hours from Triumeq is required for people who have INSTI drug resistance or are taking certain other medications.

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

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Triumeq is generally well tolerated. The most common side effects that occurred in 2–3% of study subjects are insomnia, headache, and fatigue. New data associate INSTIs and TAF with weight gain; see "Weighty Concerns," beginning on page 8, and GO TO aidsinfo.nih.gov. Dolutegravir can cause a small, reversible increase in serum creatinine within the first few weeks of treatment without affecting actual kidney function. There have been rare reports of depression and suicidal ideation, primarily in patients with a history of psychiatric illnesses, in people receiving INSTI-based regimens. The DHHS guidelines recommend closely monitoring patients with pre-existing psychiatric conditions on an INSTI. Conflicting data suggest a potential risk for heart problems when using abacavir-containing regimens in people with high risk for cardiovascular disease. Monitor for signs of hypersensitivity reaction (HSR) to abacavir. Prior to starting Triumeq, all individuals should be given a blood test for HLA-B*5701 (a genetic marker) to identify patients at risk for this reaction. This test is covered by most insurance and by LabCorp/ViiV (see company contact on co-pay chart). Read more about HSR on the Ziagen page. Prior to initiation, people should be tested for hepatitis B (HBV) infection. Severe exacerbations of hepatitis B have been reported in people who are co-infected with hepatitis B and have discontinued the lamivudine component. Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted. See "More Information."

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POTENTIAL DRUG INTERACTIONS

Do not take with the anti-arrhythmic dofetilide. Triumeq should be taken two hours before or six hours after taking antacids or laxatives, the ulcer medication Carafate, 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, Prilosec, Pepcid, Zantac, Prevacid) are okay to use. Avoid co-administration with oxcarbazepine, phenobarbital, phenytoin, or St. John's wort. Start metformin at lowest dose and titrate based on glycemic control. Monitor for metformin adverse effects. Avoid use of sorbitol-containing medicines with lamivudine; there are many, such as acetaminophen liquid (Tylenol liquid and others). Not intended to be taken with other HIV medications, unless prescribed that way. When taking rifampin, take an additional dose of dolutegravir (in the form of one Tivicay tablet) 50 mg 12 hours after taking your Triumeq dose. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Dolutegravir is now a preferred medication in pregnancy as well as an alternative drug for those who are trying to conceive, according to U.S. HIV perinatal treatment guidelines updated in December 2019 (go to aidsinfo.nih.gov/guidelines/html/3/perinatal-guidelines/0). This clears preliminary concerns over the potential for birth defects with dolutegravir, raised in 2018 by a study in Botswana. Triumeq is the only single-tablet regimen (STR) that contains Epzicom as the NRTI backbone. Compared to other INSTIs, dolutegravir has a relatively high genetic barrier against the development of drug resistance, similar to the protease inhibitors (such as Prezista). In addition, dolutegravir-containing regimens have demonstrated virologic superiority over Prezista-containing regimens. Triumeq has relatively few drug interactions and is well tolerated. Triumeq does not cover HBV as well as other STRs and therefore requires another anti-HBV medication in addition to its lamivudine component. Triumeq is a relatively large STR tablet, which can potentially be an issue for individuals who have difficulty swallowing. Other STRs containing dolutegravir are Juluca and Dovato.

DR. ROSS SLOTTEN SAYS: Like Biktarvy, Triumeq, approved in 2014, has earned an A1 rating from the DHHS expert panel. Its INSTI, dolutegravir, has a high barrier to resistance. Except in a handful of anecdotal cases, viral mutations to dolutegravir have not been detected in people who have failed therapy, although failure is usually due to noncompliance rather than drug potency. The pill itself is quite small, making it easier to take for those with pill phobia. Like Biktarvy, it's not fussy. Its absorption is not dependent on a full or empty stomach and it has few drug-to-drug interactions. The main drawback to Triumeq is that you have to test for hypersensitivity to one of its components, abacavir. ViiV, its manufacturer, claims that such hypersensitivity is rare, but I've detected it on a number of occasions, more frequently than I was led to expect. The reaction is potentially dangerous, even life-threatening, so testing for the genetic marker HLA-B*5701 is essential before prescribing it. Another concern is the risk of a cardiovascular event, like a heart attack, especially after initiating therapy. On this issue, the data are conflicting. No randomized controlled study to prove a cause and effect relationship has been conducted. Competitors have exploited this gray area and given the drug an undeserved bad rap, but all is fair in war (whether against HIV or a pharmaceutical opponent). Dolutegravir should not be used in the first trimester (14 weeks) of pregnancy because of potential neural tube defects; but it is one of the preferred treatments in the second and third trimesters of pregnancy. Like Biktarvy, this is an excellent first-line therapy.

ACTIVIST BRIDGETTE PICOU SAYS: Another single-tablet regimen, Triumeq requires a specific blood test because of the abacavir component. If you have the genetic sensitivity the test looks for—called HLA-B*5701—you cannot take Triumeq. You should also know that if you develop an allergy, stop taking the drug and notify your doctor. You should not take the medication again. There has been discussion of the abacavir component and cardiac concerns. You can discuss this and other risks and benefits with your doctor. Triumeq may cause a feeling of being tired, or may also cause insomnia. Adjusting the time of day you take it may help with these effects.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$3,638.51/MONTH

Dovato

DTG/3TC
dolutegravir/lamivudine

STR — SINGLE-TABLET REGIMEN CONTAINING AN INSTI AND AN NRTI

★ RECOMMENDED INITIAL REGIMEN FOR MOST PEOPLE EXCEPT THOSE WITH VIRAL LOAD GREATER THAN 500,000 COPIES/ML, HBV CO-INFECTION, OR BEFORE RESULTS OF GENOTYPIC RESISTANCE OR HBV TESTING

STANDARD DOSE

One tablet once daily, without regard to food for treatment-naïve people who have no known resistance to the dolutegravir and lamivudine components of the regimen. Tablet contains 50 mg of the INSTI dolutegravir plus 300 mg of the NRTI lamivudine.

Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. See package insert when available for guidance on dosing in the setting of kidney impairment. Dovato is not recommended for people who have a CrCl less than 50 mL/min or who have severe liver impairment.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Dolutegravir and lamivudine are both generally well tolerated. Side effects occurring in at least 2% of study participants receiving Dovato included headache, nausea, diarrhea, insomnia, fatigue, and dizziness. New data associate INSTIs and TAF with weight gain; see "Weighty Concerns," beginning on page 8, and GO TO aidsinfo.nih.gov. Dolutegravir can cause a small, reversible increase in kidney function test (serum creatinine) within the first few weeks of treatment without affecting actual kidney function. There have been rare reports of depression and suicidal ideation, primarily in patients with a history of psychiatric illnesses, in people receiving INSTI-based regimens. The DHHS guidelines recommend closely monitoring patients with pre-existing psychiatric conditions on an INSTI. Liver enzymes should be monitored in people with hepatitis B or C and taking dolutegravir. 3TC can treat both HIV and HBV, but must be used in combination with another hep B drug (such as tenofovir) to treat the hep B. If you are co-infected with HBV and HIV, you should not stop 3TC without medical supervision because it can cause your HBV to flare and cause you to experience signs and symptoms of acute hepatitis. HBV should be closely monitored by your provider.

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POTENTIAL DRUG INTERACTIONS

Do not take Dovato with Epivir-HBV. When taking carbamazepine or rifampin, take an additional dose of dolutegravir (in the form of one Tivicay tablet) 50mg 12 hours after taking your Dovato dose. When starting or stopping dolutegravir in people on metformin, dose adjustment of metformin may be necessary to maintain optimal glycemic control. Avoid use of sorbitol-containing medicines with lamivudine; there are many, such as acetaminophen liquid (Tylenol liquid and others). Should be okay to take with Daklinza, Epclusa, Harvoni, Olysio, Sovaldi, Viekira Pak, or Zepatier. Not intended to be taken with other HIV medications, unless prescribed that way. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Approved in April 2019. Basically, this medicine is Triumeq without the abacavir component (brand name Ziagen, also found in Epzicom). Dolutegravir is from the powerhouse drug class of integrase inhibitors, which are highly effective and generally tolerable. The benefits of using a two-drug regimen for HIV include less exposure to HIV medication while maintaining viral suppression and also minimizing the potential for side effects. At one year in the GEMINI-1 and GEMINI-2 studies, DTG plus 3TC was found to be non-inferior to the triple drug regimen of DTG plus Truvada (emtricitabine and tenofovir DF combined in one pill). For the two studies, 91% (655 out of 716 individuals) had undetectable viral load, compared to 93% (669 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). Results from week 48 study called TANGO evaluated treatment switch from TAF-containing regimens with three or more drugs to the 2-drug regimen of dolutegravir/lamivudine. Dolutegravir is now a preferred medication in pregnancy as well as an alternative drug for those who are trying to conceive, according to U.S. HIV perinatal treatment guidelines updated in December 2019 (GO TO aidsinfo.nih.gov/guidelines/html/3/perinatal-guidelines/0). This clears preliminary concerns over the potential for birth defects with dolutegravir raised in 2018 by a study in Botswana.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com
(877) 844-8872

DR. ROSS SLOTTEN SAYS: Dovato is an intriguing STR approved for treatment-naïve individuals. It contains only two drugs, dolutegravir and the NRTI lamivudine (3TC). In clinical trials, it has been shown to be equivalent in potency to 3-drug combinations in patients who have never been treated for HIV in the past. Its primary virtue is that it doesn't contain TDF, with its risks for kidney toxicity and loss of bone density. Except in patients who can't tolerate or in whom TDF (or TAF) is contraindicated, like people with chronic kidney disease (even TAF-containing regimens should only be prescribed for patients with a creatinine clearance of greater than 30 mL/minute), its role is limited.

ACTIVIST BRIDGETTE PICOU SAYS: HIV treatment modalities have changed over the years, and continue to change rapidly with research. While once waiting for CD4 counts to drop into the low 200s, we are now starting within days of diagnosis; we've gone from multiple drugs multiple times a day, to more simplified regimens. Enter Dovato. The second two-drug STR option on the market, the concept is still fairly new, but clinical trials have shown it to be non-inferior to three-drug combos. Less drug translates into less drug toxicity in the long term. That's a definite plus considering people are living 30-plus years with HIV. Gaining popularity as a rapid start option, the components offer a high barrier for resistance with minimal side effects reported.

AVERAGE WHOLESALE PRICE

$2,890.04/MONTH

Juluca DTG/RPV
dolutegravir/rilpivirine

STR SINGLE-TABLET REGIMEN CONTAINING AN INSTI AND AN NNRTI

✔ RECOMMENDED AS CONTINUATION THERAPY FOR PEOPLE WITH UNDETECTABLE HIV VIRAL LOAD FOR AT LEAST 6 MONTHS

STANDARD DOSE

One tablet once daily, with a meal (see Edurant), for adults who are virologically suppressed (have an undetectable viral load of less than 50 copies per mL) on a current ART (antiretroviral therapy) regimen for at least 6 months and who have no history of treatment failure or resistance mutations associated with rilpivirine or dolutegravir. Tablet contains 50 mg of the INSTI dolutegravir plus 25 mg of the NNRTI rilpivirine.

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

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Both dolutegravir and rilpivirine are generally well tolerated. Side effects observed in greater than 2% of study participants were diarrhea and headache. New data associate INSTIs and TAF with weight gain; see "Weighty Concerns," beginning on page 8, and GO TO aidsinfo.nih.gov. Dolutegravir and rilpivirine can each cause a small, reversible increase in a kidney function test (serum creatinine) within the first few weeks of treatment without affecting actual kidney function. There have been rare reports of depression and suicidal ideation, primarily in patients with a history of psychiatric illnesses, in people receiving INSTI-based regimens. The DHHS guidelines recommend closely monitoring patients with pre-existing psychiatric conditions on an INSTI. Liver enzymes should be monitored in people with hepatitis B or C and taking dolutegravir. Call your health care provider right away if you develop any of the following signs or symptoms: yellowing of the skin or whites of the eyes; dark or tea-colored urine; pale-colored bowel movements; nausea or vomiting; loss of appetite; or pain, aching, or tenderness on the right side below the ribs.

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POTENTIAL DRUG INTERACTIONS

Do not take Juluca with the anti-arrhythmic dofetilide. If taking rifabutin, add an Edurant tablet to Juluca dose. If you take antacids, laxatives, or other products that contain aluminum, calcium carbonate, magnesium, or buffered medicines, Juluca should be taken (with a meal, as always) at least 4 hours before or 6 hours after you take these medicines. Alternatively, these medications can be taken at the same time with Juluca and the meal. Take Juluca with a meal 4 hours before or 12 hours after you take H2 blocker acid reducers (Pepcid, Zantac, Tagamet) or buffered medications. Juluca should not be taken with proton pump inhibitors (such as Aciphex, Dexilant, Prilosec, Prevacid, Protonix, Nexium). Avoid taking Juluca with some seizure medicines (carbamazepine, oxcarbazepine, phenobarbital, and phenytoin) or St. John's wort. HIV treatment guidelines suggest that metformin be started at the lowest dose and titrated based on glycemic control. Monitor for metformin adverse effects. When starting or stopping Juluca in people on 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. When taking rifampin, take an additional dose of dolutegravir (in the form of one Tivicay tablet) 50 mg 12 hours after taking your Juluca dose. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Juluca was the first two-drug combination approved as a complete regimen for HIV. It replaces a three- or four-drug therapy for people with undetectable viral loads who want to switch to a simpler or smaller tablet regimen. People switching to Juluca must be virologically suppressed (with viral loads of less than 50 copies per mL) on a stable antiretroviral regimen for at least six months. This is a new HIV treatment strategy and potentially a game changer, especially with other dual-drug antiviral medications on the way. Those able to take their medications correctly, consistently, and achieve undetectable viral load can take advantage of this drug-sparing strategy. Currently people taking HIV treatment must start out with a three-drug regimen (which may include the use of one of the single-tablet regimens, or STRs), then switch to Juluca after being undetectable for six months. Juluca still works against two steps of the life cycle of the virus, similar to 3-drug regimens. This is how the combination was used in clinical studies to date. This combination was listed in U.S. HIV guidelines as a "Strategy with good supporting evidence" around the time of its FDA approval. The guidelines also called Juluca "a reasonable option when using nucleoside drugs is not desirable" (for example, due to previous toxicity), with an A1 rating (strong recommendation based on randomized controlled trials). Juluca is the first nucleoside-free STR. Currently, all the STRs except Dovato and Juluca contain two nucleoside drugs. Juluca contains two currently available medications. The benefits of taking Juluca include less exposure to HIV medications while maintaining viral suppression. Juluca is the smallest STR, which may be advantageous to individuals who have difficulty swallowing. Dolutegravir is now a preferred medication in pregnancy as well as an alternative drug for those who are trying to conceive, according to U.S. HIV perinatal treatment guidelines updated in December 2019 (GO TO aidsinfo.nih.gov/guidelines/html/3/perinatal-guidelines/0). This clears preliminary concerns over the potential for birth defects with dolutegravir raised in 2018 by a study in Botswana.

DR. ROSS SLOTTEN SAYS: Approved in 2017, Juluca is another highly effective STR, but it does not include 2 NRTIs. It is a unique two-drug regimen: an INSTI and NNRTI (non-nucleoside reverse transcriptase inhibitor). NRTIs have been implicated in a number of adverse events, like lactose acidosis (all NRTIs), kidney toxicity (TDF), lipodystrophy (AZT/Retrovir and D4T/Zerit), heart attacks (abacavir), and bone density loss (TDF). Juluca contains dolutegravir and rilpivirine, a second generation non-nucleoside reverse transcriptase inhibitor distantly related to efavirenz (Sustiva). The drug has a special place in my heart because it is the first STR that I have been able to prescribe to people who were heavily pre-treated in the early days of HIV treatment and developed multiple resistance mutations to the NRTI class of drugs. Thus, Biktarvy and Triumeq, yet to be proven otherwise, are probably not good choices in this setting. It is very well tolerated and, like Triumeq, a very tiny pill. The main drawback to Juluca is that rilpivirine has a low barrier to resistance. The medication must be taken with a high caloric meal (more than 400 calories) that must be chewed (no protein drinks; chewing increases its absorption). It can't be taken with a proton pump inhibitor (PPI), like Prilosec, Nexium, or Prevacid, which interferes with rilpivirine's absorption. Other acid blockers, like Tagamet, Pepcid, and Zantac, will not interfere with absorption if taken 12 hours apart. Juluca is a niche drug but one that has reduced the pill burden in a number of my heavily pre-treated patients.

ACTIVIST BRIDGETTE PICOU SAYS: Juluca is indicated as a switch regimen. Specifically, patients virally suppressed for more than six months and stable on their current regimen. It is two drugs rather than three, which is a long-term-use benefit since it should reduce drug effects on the body over time. Less drug, less toxicity. Juluca should also be taken with a meal.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com
(877) 844-8872

AVERAGE WHOLESALE PRICE

$3,410.06/MONTH

Symtuza

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

STR SINGLE-TABLET REGIMEN CONTAINING A PROTEASE INHIBITOR, A PHARMACOKINETIC ENHANCER (BOOSTER), AND TWO NRTIs

✔ RECOMMENDED INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

One tablet once daily with food for treatment-naïve people or people with suppressed viral load on a stable HIV regimen for at least 6 months who have no known resistance to the darunavir or tenofovir components of the regimen. Tablet contains 800 mg darunavir, 150 mg cobicistat, 200 mg emtricitabine, and 10 mg tenofovir alafenamide.

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 in people with an estimated creatinine clearance of at least 30 mL/min. It should not be used in people with severe kidney or liver impairment.

- SEE THE INDIVIDUAL DRUGS CONTAINED IN SYMTUZA: Prezista, Tybost, and Descovy.
- SEE PACKAGE INSERT for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

As darunavir contains a sulfa component, use with caution in patients with sulfa allergies. Side effects most commonly reported in studied subjects include diarrhea (9%), rash (8%), nausea (6%), fatigue (4%), headache (3%), abdominal discomfort (2%), and flatulence (2%). New data associate INSTIs and TAF with weight gain; see "Weighty Concerns," beginning on page 8, and GO TO aidsinfo.nih.gov. While very rare, severe rash, accompanied in some cases by fever and/or elevations of AST/ALT (liver enzymes), can be life-threatening. Seek medical attention immediately. Observational cohort studies reported an association between some PIs (including darunavir when given with Norvir) and an increased risk of cardiovascular (CV) events, but data with darunavir/cobicistat is too limited to see such a connection. With PIs, there can be increased bleeding in hemophiliacs. Cobicistat can cause a small, reversible increase in serum creatinine (SCr, which indicates the eGFR or estimated CrCl lab values) within the first few weeks of treatment without affecting actual kidney function (see Tybost for more information). Patients experiencing a confirmed increase in serum creatinine of greater than 0.4 mg/dL from baseline should be closely monitored for renal safety. Serum phosphorus in patients with or at risk for kidney impairment should also be monitored. Prior to initiation, people should be tested for hepatitis B (HBV) infection. Severe exacerbations of hepatitis B have been reported in people who are co-infected with hepatitis B and have discontinued the emtricitabine and/or tenofovir components. Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted. Although some older PIs have been associated with liver toxicity, lactic acidosis, diabetes, or fat redistribution, these conditions are only rarely, or never, seen with darunavir. IRIS (immune reconstitution inflammatory syndrome) may occur as the immune system regains strength; signs and symptoms from previous infections may occur soon after HIV treatment is initiated. Report symptoms of illness, such as shingles or TB, to a health care provider.

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POTENTIAL DRUG INTERACTIONS

Do not take with Epivir-HBV, Hepsera, or Vemlidy (TAF), all three used for the treatment of hepatitis B. Use with other protease inhibitors or Intelence, Sustiva, or Viramune is not recommended. Do not take with betamethasone, budesonide, carbamazepine, dexamethasone, dronedarone, eslicarbazepine, ergot derivatives, fluticasone, triazolam, oral midazolam, lurasidone, methylprednisolone, oxcarbazepine, phenobarbital, phenytoin, pimozide, Revatio, simvastatin, lovastatin, St. John's wort, alfuzosin, ranolazine, or rifampin. Not recommended to be taken with apixaban, avanafil, dabigatran etexilate (in renal impairment), everolimus, rifampentine, rivaroxaban, salmeterol, ticagrelor, or voriconazole. Beclomethasone and prednisone as alternative corticosteriods 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. Do not take with colchicine if there is kidney or liver impairment. Cannot be taken with Zepatier. Based on the mechanism, drug interactions with other hepatitis C medications are probably similar to the interactions with Prezista + Norvir + Descovy. Not intended to be taken with other HIV medications, unless prescribed that way. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

This medication was approved in 2018 and is the first STR containing a protease inhibitor. This formulation is much more convenient and reduces the number of co-pays to one. It is not the same as Prezcobix plus Descovy, because Symtuza contains a lower dose of TAF than Descovy. A benefit of the PIs is their high genetic barrier to the development of drug resistance. While medical providers may hate to say it out loud, this means greater forgiveness of missed doses; missing a dose here and there is never advisable but does happen. As such, a PI-based regimen such as Symtuza suits some people who may have trouble with the near-perfect drug adherence required of HIV treatment. In fact, the FDA allowed Janssen to advertise Symtuza as "help[s] protect against resistance." Symtuza may be used in rapid initiation, treatment given within 7 days of HIV diagnosis, before resistance test results are available. Treatment-experienced individuals with undetectable viral loads for at least six months may switch to Symtuza. Darunavir is available under the brand name Prezista and is also found in the co-formulated pill Prezcobix (with cobicistat). Symtuza is not recommended during pregnancy due to substantially lower exposures of darunavir and cobicistat components during pregnancy. Compared with tenofovir DF, the tenofovir alafenamide in Symtuza is safer on kidney and bone health. Also as a result of the TAF, Symtuza can be taken by people with more advanced kidney disease, down to a renal function (CrCL) of 30 mL/min.

DR. ROSS SLOTTEN SAYS: FDA-approved in July 2018, Symtuza contains the protease inhibitor darunavir (Prezista), boosting agent cobicistat, and 2 NRTIs (TAF and FTC). Because of the presence of cobicistat, it will not be considered an A1 agent by DHHS. Symtuza is the first and perhaps last STR containing a PI, at least for the foreseeable future unless a PI can be found that doesn't require boosting. That said, I don't see a special role for this medication, except for people who are already on Prezista and 2 NRTIs, and for those patients who may not be ideally adherent to their HIV regimen because darunavir has a high barrier to resistance, if one believes that PIs are superior to INSTIs in this scenario. I'm not knocking Symtuza. It's as potent as Biktarvy and Triumeq but the presence of a boosting agent increases the chances of drug-to-drug interactions. It also has more side effects, mainly GI, than INSTI-containing regimens.

ACTIVIST BRIDGETTE PICOU SAYS: Symtuza is considered unique because it is the only boosted protease inhibitor single-tablet regimen (STR). It can be used as both a start therapy regimen and also as a switch option for those who are stable with no resistance. This medication should be taken with food, or within half an hour or so of eating. The darunavir component has a high barrier to resistance. There are drug-drug interactions to consider so discuss your medications with your doctor since the booster component of Symtuza may affect how well they work.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$4,667.71/MONTH

Delstrigo

DOR/3TC/TDF
doravirine/lamivudine/tenofovir DF

STR — SINGLE-TABLET REGIMEN CONTAINING AN NNRTI AND TWO NRTIs

✔ RECOMMENDED INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

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

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

- SEE THE INDIVIDUAL DRUGS CONTAINED IN DELSTRIGO: Pifeltro, Viread, and Epivir.
- 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 of people taking it were dizziness (7%), nausea (5%), abnormal dreams (5%), and headache (4%). In one study (DRIVE-AHEAD), an in-depth analysis was conducted of the incidence of neuropsychiatric adverse events associated with Delstrigo compared to Atripla. Neuropsychiatric events, such as depression, sleep disturbances, dizziness, etc., are another common side effect of the NNRTI class. The proportion of subjects who reported one or more neuropsychiatric adverse events overall was 24% for the Delstrigo group compared to 57% for the Atripla group. The neuropsychiatric adverse events associated with depression and suicide/self-injury were reported in 4% of the Delstrigo group compared to 7% of the Atripla group. Overall, sleep disturbances (e.g., abnormal dreams, insomnia, nightmares, etc.) were associated with 12% of people in the Delstrigo group compared to 26% of people in the Atripla group. Dizziness was associated with 9% in the Delstrigo group compared to 37% of the Atripla group. Altered sensorium (e.g., lethargy, drowsiness, etc.) was associated with 4% of people in the Delstrigo group compared to 8% of people in the Atripla group. 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 patients on TDF-containing regimens. BMD monitoring should be considered in people who have a history of bone fracture due to bone disease or are at risk for osteopenia or osteoporosis. TDF may cause kidney toxicities. Creatinine clearance (CrCl) should be assessed before initiating treatment. In addition to CrCl, glucose and protein in the urine and serum phosphorus should be monitored more often in patients at risk for kidney problems. Tell your provider about any pain in extremities, persistent or worsening bone pain and fractures, with or without muscular pain or weakness, as well as any concerning changes in urinary habits, as these could be signs of kidney problems. If you have HIV and HBV, guidelines recommend treatment for both viruses. Delstrigo can be used to treat HIV and HBV simultaneously. If you are co-infected with HBV and HIV, you should not stop Delstrigo without medical supervision because it can cause your HBV to flare and cause you to experience signs and symptoms of acute hepatitis. HBV should be closely monitored by your provider.

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POTENTIAL DRUG INTERACTIONS

Do not take with Epivir-HBV, Hepsera, or Vemlidy (TAF), all three used for hepatitis B. When using with the antibiotic drug rifabutin (used for TB and to prevent MAC in AIDS patients), increase the doravirine dose by adding a Pifeltro tablet approximately 12 hours later. 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 (cancer drug) mitotane; and the herbal St. John's wort. Avoid use of sorbitol-containing medicines with lamivudine; there are many, such as acetaminophen liquid (Tylenol liquid and others). Epclusa and Harvoni each increase the concentration of TDF; monitor for adverse reactions. Not intended to be taken with other HIV medications, unless prescribed that way. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Stand-alone versions of doravirine (Pifeltro) and lamivudine/tenofovir DF (Cimduo, Temixys) were also approved; see those pages. Unfortunately, Delstrigo contains an older version of tenofovir, TDF. A safer version, TAF, is available and used in some STRs. Ironically, however, as TAF and INSTIs may have some association with weight gain (see "Weighty Concerns," beginning on page 8, and GO TO aidsinfo.nih.gov), Delstrigo may become a more popular option. TDF is still an effective and quite tolerable medication, but TAF has potentially less renal and bone toxicity. Doravirine has not been directly compared to integrase inhibitor-based regimens in clinical trials yet. There is no data on the safety of Delstrigo use in pregnancy.

DR. ROSS SLOTTEN SAYS: Delstrigo, another STR, was approved by the FDA in August 2018. It has been described as a "quasi" generic because two of its components, TDF and 3TC (Epivir/lamivudine) are generic. Doravirine is a "second generation" NNRTI, distantly related to efavirenz. Delstrigo has earned a B1 rating from the DHHS, which means that it is moderately recommended and has been shown in non-randomized trials to be "non-inferior" to efavirenz- or darunavir-containing regimens. There have been no head-to-head clinical trials comparing this medication to INSTI-containing regimens. In terms of potency, it's equivalent to many other HAART regimens. It contains TDF and not TAF. Currently, there is a class action lawsuit against Gilead, the manufacturer of TDF-containing regimens for "bone fracture" and "kidney injury." Although, in my opinion, such a lawsuit is ridiculous, given that HIV medications have saved people's lives and caused more good than harm, why would we now prescribe this medication as a first-line agent or a switch from another regimen when we have alternatives that either contain a TAF component or neither TAF nor TDF? Moreover, doravarine has a relatively low barrier to resistance and treatment-emergent resistance has been observed. I would classify this medication as a "C," if asked, "C" meaning compelled by an insurance company for cost reasons only to prescribe it.

ACTIVIST BRIDGETTE PICOU SAYS: Delstrigo is a single-tablet regimen that can be taken with or without food. While it should not be used if there is moderate to severe kidney impairment, it seems otherwise tolerated well and considered safe. You should be tested for hepatitis B before starting or stopping this medication. If you are hep B-positive you can still take Delstrigo, but do not stop it suddenly or without notifying your provider as it may cause a harmful flare-up of your HBV infection. This medication can be used in both treatment-naïve (new starts) and treatment-experienced (stable regimen switch) individuals.

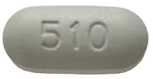
In the DRIVE-FORWARD study comparing doravirine to darunavir, results for the treatment-naïve individuals in the study were 80% (darunavir group) and 84% (doravirine group) undetectable (less than 50 viral load).

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$2,646.00/MONTH



Genvoya

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

STR — SINGLE-TABLET REGIMEN CONTAINING A BOOSTED INSTI AND TWO NRTIs

✔ RECOMMENDED INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

One tablet once daily with food. For people taking HIV treatment for the first time (treatment-naïve) or individuals with suppressed viral load on a stable HIV regimen for at least 6 months who have no known resistance to the elvitegravir, emtricitabine, or tenofovir components of the regimen. Tablet contains 150 mg of the INSTI elvitegravir boosted by 150 mg cobicistat plus 200 mg emtricitabine and 10 mg tenofovir alafenamide (TAF).

For adults and children weighing at least 55 pounds (25 kg) and having a creatinine clearance 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 those on HD, take tablet once daily and administer after completion of hemodialysis on days of HD treatment.

Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. Dose cannot be adjusted for people with liver problems. Genvoya is not recommended for people who have severe liver problems, a CrCl between 15 to 30 mL/min, or a CrCl less than 15 mL/min who are not receiving chronic hemodialysis.

- **SEE THE INDIVIDUAL DRUGS CONTAINED IN GENVOYA:** Emtriva and Tybost (elvitegravir is not available separately, and neither is TAF for use in HIV, but see Descovy).
- **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

Common side effects reported in at least 5% of study participants include nausea, diarrhea, headache, and fatigue. New data associate INSTIs and TAF with weight gain; see "Weighty Concerns," beginning on page 8, and **GO TO** aidsinfo.nih.gov. Before taking Genvoya, kidney function testing should be conducted, including serum creatinine (SCr), serum phosphorus, urine glucose, and urine protein. These measurements should continue to be monitored while taking Genvoya. Cobicistat can cause a small, reversible increase in serum creatinine within the first few weeks of treatment without affecting actual kidney function (see Tybost for more information). While cobicistat does not affect actual kidney function, its effect on SCr can make monitoring of impaired kidney function more difficult or less accurate. INSTIs have been associated with adverse neuropsychiatric effects (such as sleep disturbances, depression, anxiety, suicidal ideation) in some retrospective cohort studies and case series. The DHHS guidelines recommend closely monitoring patients on an INSTI who have pre-existing psychiatric conditions. Prior to initiation, people should be tested for hepatitis B (HBV) infection. Severe exacerbations of hepatitis B have been reported in people who are co-infected with hepatitis B and have discontinued the emtricitabine and/or tenofovir components. Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted.

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POTENTIAL DRUG INTERACTIONS

Do not take with Epivir-HBV, Hepsera, or Vemlidy (TAF), all three used for the treatment of hepatitis B. Separate by at least 2 hours from antacids containing aluminum, magnesium hydroxide, or calcium carbonate. Safe to take with other medications used for heartburn and GERD such as Nexium, Pepcid, Prevacid, Prilosec, and Zantac. Cobicistat has many drug interactions similar to Norvir. Do not take with cholesterol-lowering drugs containing lovastatin or simvastatin (Advicor, Altoprev, Mevacor, Simcor, Vytorin, Zocor), alfuzosin, carbamazepine, phenobarbital, phenytoin, ergotamine, dihydroergotamine, methylergonovine, oral midazolam, lurasidone, pimozide, Revatio, rifampin, rifabutin, rifapentine, Serevent, triazolam, or St. John's wort. Dose of clarithromycin may need to be reduced based on kidney function. An alternative corticosteroid to systemic dexamethasone should be considered. Risks versus benefits of using with voriconazole should be assessed with expert consultation. Some cholesterol-lowering drugs such as atorvastatin should be used with caution and started at the lowest dose possible. Monitor closely for increased side effects from these medications, such as muscle pain. Concentrations of antidepressants such as fluoxetine, paroxetine, bupropion, or amitriptyline may be increased, and their doses may need to be reduced. Genvoya increases levels of many nasal and inhaled steroids like fluticasone, which may lead to symptoms of Cushing's syndrome. An alternative corticosteroid to fluticasone is recommended. Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours. Monitor for increased side effects of these medications. Effectiveness of oral contraceptives may be decreased; consider using alternative or additional contraception methods. Reduce Daklinza dose to 30 mg. Can be taken with Harvoni. Taking with Olysio, Viekira Pak, or Zepatier is not recommended. Monitor kidney function more closely with Epclusa. Not intended to be taken with other HIV medications, unless prescribed that way. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are many other drug interactions not listed here.

DR. ROSS SLOTTEN SAYS: Before Biktarvy, Genvoya was one of my "go-to" drugs. It contains TAF, which has less potential for kidney toxicity and bone density loss than TDF-containing regimens like Atripla or Stribild. But now that Biktarvy is available, there's no reason to prescribe Genvoya as a first-line therapy. And, in fact, it has dropped from A1 status to B1. For those individuals already on Genvoya who have no significant co-morbidities, I have not made the switch to Biktarvy. At this point, there's absolutely no compelling reason to do so. It is an excellent drug, with few side effects and high potency.

ACTIVIST BRIDGETTE PICOU SAYS: This single-tablet regimen came out in 2015 and was an "update" so to speak to Stribild. Containing TAF (tenofovir alafenamide fumarate), Genvoya is considered less bone and kidney toxic. Since it also contains the booster cobicistat, consideration should be given if you take certain other medications. Discuss all medicines and anything you take over the counter with your doctor before starting it, and if prescribed new medication from an outside physician.

MORE INFORMATION

Genvoya is not recommended for use in pregnancy due to substantially lower exposures of cobicistat and elvitegravir during the second and third trimesters as well as reports of viral breakthrough. Switching regimens should be considered for pregnant women already taking this regimen.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$3,885.97/MONTH

Stribild

EVG/COBI/FTC/TDF
elvitegravir/cobicistat/emtricitabine/tenofovir DF

STR SINGLE-TABLET REGIMEN CONTAINING A BOOSTED INSTI AND TWO NRTIs

✔ RECOMMENDED INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

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

For adults and children 12 years of age and older weighing 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. Dose cannot be adjusted for people with kidney or liver problems. Stribild should not be started in individuals with estimated CrCl less than 70 mL/min and should be discontinued if CrCl decreases to less than 50 mL/min. Stribild is not recommended for patients with severe liver problems, or during pregnancy.

- **SEE THE INDIVIDUAL DRUGS CONTAINED IN STRIBILD:** Emtriva, Viread, and Tybost (elvitegravir is not available separately).
- **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

Common side effects reported in 10% or more of study participants include nausea and diarrhea. Other less common side effects include abnormal dreams and headache. New data associate INSTIs and TAF with weight gain; see "Weighty Concerns," beginning on page 8, and GO TO aidsinfo.nih.gov. Before taking Stribild, kidney function testing should be conducted including serum creatinine, serum phosphorus, urine glucose, and urine protein. These measurements should continue to be monitored while taking Stribild. Cobicistat can cause a small, reversible increase in serum creatinine within the first few weeks of treatment without affecting actual kidney function (see Tybost for more information). There have been rare reports of depression and suicidal ideation, primarily in patients with a history of psychiatric illnesses, in people receiving INSTI-based regimens. The DHHS guidelines recommend closely monitoring patients on an INSTI who have pre-existing psychiatric conditions. Prior to initiation, people should be tested for hepatitis B (HBV) infection. Severe exacerbations of hepatitis B have been reported in people who are co-infected with hepatitis B and have discontinued the emtricitabine and/or tenofovir components. Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted.

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POTENTIAL DRUG INTERACTIONS

Do not take with Epivir-HBV, Hepsera, or Vemlidy (TAF), all three used for the treatment of hepatitis B. Separate by at least 2 hours from antacids containing aluminum, magnesium hydroxide, or calcium carbonate. Stribild is safe to take with other medications used for heartburn and GERD, such as Nexium, Pepcid, Prevacid, Prilosec, and Zantac. Do not take Stribild with alfuzosin, carbamazepine, phenobarbital, phenytoin, ergotamine, dihydroergotamine, methylergonovine, oral midazolam, pimozide, Revatio, rifampin, rifabutin, rifapentine, Serevent, triazolam, or St. John's wort. An alternative corticosteroid to systemic dexamethasone should be considered. No significant interactions with beclomethasone or prednisolone. Risks versus benefits of using Stribild and voriconazole together should be assessed with expert consultation. Do not use with lovastatin or simvastatin (Advicor, Altoprev, Mevacor, Simcor, Vytorin, and Zocor). Cholesterol-lowering drugs such as rosuvastatin and atorvastatin should be used with caution and started at the lowest dose possible. Monitor closely for increased side effects from these medications, such as muscle pain. Concentrations of antidepressants such as fluoxetine, paroxetine, bupropion, or amitriptyline may be increased by Stribild, and their doses may need to be reduced. Use with caution and therapeutic monitoring, if available, for antiarrhythmic drugs like digoxin. Stribild increases levels of many nasal and inhaled steroids like fluticasone, which may lead to symptoms of Cushing's syndrome. An alternative corticosteroid to fluticasone is recommended. Use caution with beta blockers and calcium channel blockers. Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours. Monitor for increased side effects of these medications, such as visual disturbances. Effectiveness of oral contraceptives may be decreased; consider using alternative or additional contraception methods. Co-administer bosentan and immunosuppressants like Prograf, Gengraf, Neoral, and Sandimmune with caution. Reduce Daklinza dose to 30 mg. Taking with Harvoni, Olysio, Viekira Pak, or Zepatier is not recommended. Monitor kidney function more closely with Epclusa. Not intended to be taken with other HIV medications, unless prescribed that way. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are many other drug interactions not listed here.

DR. ROSS SLOTTEN SAYS: No comment provided because it has been replaced by Genvoya.

ACTIVIST BRIDGETTE PICOU SAYS: Stribild is one of the regimens that should be taken with food. A single-tablet regimen, it contains the original tenofovir formulation TDF, making monitoring of your bone and kidney function necessary. Additionally, the booster cobicistat means being aware of and monitoring for drug-drug interactions with some commonly used drugs like statins and erectile dysfunction medications.

MORE INFORMATION

Stribild is not recommended for use in pregnancy due to substantially lower exposures of cobicistat and elvitegravir during the second and third trimesters as well as reports of viral breakthrough. Switching regimen or close monitoring should be considered for pregnant women already taking this regimen.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$4,076.39/MONTH

Odefsey

RPV/FTC/TAF
rilpivirine/emtricitabine/tenofovir alafenamide

STR SINGLE-TABLET REGIMEN CONTAINING AN NNRTI AND TWO NRTIs

✔ RECOMMENDED INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

One tablet once daily, with a standard meal (more than 390 calories). For people taking HIV therapy for the first time (treatment-naïve) or people with suppressed viral load on a stable HIV regimen for at least 6 months who have no known resistance to the rilpivirine, emtricitabine, or tenofovir components of the regimen. See below. Tablet contains 25 mg of the NNRTI rilpivirine plus 200 mg emtricitabine and 25 mg tenofovir alafenamide (TAF).

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

People taking HIV treatment for the first time must have an HIV RNA (viral load) of less than 100,000 copies/mL and a CD4 T cell count of more than 200 cells/mm^3 before starting Odefsey due to higher rates of virologic failure in these patients.

For adults and children 12 years of age and older weighing at least 77 pounds (35 kg) and having a CrCl of at least 30 mL/min, or people with a CrCl less than 15 mL/min who are receiving dialysis.

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

➤ **SEE THE INDIVIDUAL DRUGS CONTAINED IN ODEFSEY:** Edurant and Descovy (co-formulation of Emtriva and TAF).

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Moderate to severe side effects are uncommon; insomnia, headache, and depressive disorders (depression, negative thoughts, suicidal thoughts or actions) were each reported in 2% of study participants on rilpivirine-containing regimens. Cases of rash, angioedema (swelling), urticaria (itchy rash), and increased liver enzymes have also been reported with regimens containing rilpivirine. There may be a small increase in serum creatinine (SCr) and decrease in estimated creatinine clearance (CrCl) associated with rilpivirine. See Descovy page for other possible effects on kidney function. The most common (greater than 10%) side effect seen in clinical trials with Descovy (the fixed-dose combination of Emtriva and TAF) is nausea. Prior to initiation, people should be tested for hepatitis B (HBV) infection. Severe exacerbations of hepatitis B have been reported in people who are co-infected with hepatitis B and have discontinued the emtricitabine and/or tenofovir components. Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted.

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POTENTIAL DRUG INTERACTIONS

Do not take with Epivir-HBV, Hepsera, or Vemlidy (TAF), all three used for the treatment of hepatitis B. Proton pump inhibitors (PPIs, heartburn or stomach acid drugs like Aciphex, Dexilant, Nexium, Prevacid, Prilosec, Protonix, etc.) can't be taken with Odefsey. Antacids containing aluminum, magnesium hydroxide, or calcium carbonate can be taken two hours before or four hours after Odefsey. Stomach acid-reducing drugs like Pepcid, Tagamet, and Zantac can be taken 12 hours before or four hours after a dose of Odefsey. Do not take with carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifampin, rifapentine, or the herb St. John's wort. Taking Odefsey with rifabutin is not recommended. Do not take with more than one dose of the injectable steroid dexamethasone (sometimes given in the ER or hospital). Use caution if used with fluconazole, itraconazole, ketoconazole, posaconazole, and voriconazole. Use azithromycin when possible instead of the antibiotics clarithromycin, erythromycin, or telithromycin, because these drugs increase rilpivirine levels, which can increase the risk for side effects. Reduced methadone levels can occur and while dose adjustments are not necessary, it is recommended to monitor for withdrawal symptoms. Odefsey should also not be taken with other medications that prolong QTc interval or medications with a known risk of torsades de pointes. May be taken with Harvoni, Zepatier, or Epclusa. Not intended to be taken with other HIV medications, unless prescribed that way. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Odefsey is a single-tablet regimen that is an option for people with impaired kidney function. Rilpivirine-containing regimens can be relatively difficult to take because of their food requirement and drug interactions. In addition, strict adherence is critical due to the relatively low barrier to the development of resistance. The Odefsey tablet is very small in size, which may be advantageous to individuals who have difficulty swallowing. For pregnant patients who are already on Odefsey prior to pregnancy and who are virologically suppressed, one tablet taken once daily may be continued. Lower exposures of rilpivirine were observed during pregnancy, therefore viral load should be monitored closely.

DR. ROSS SLOTTEN SAYS: Approved in 2016, Odesfey is another excellent STR. It is well tolerated and has few side effects. Its main deficiencies are that it is has to be taken with a high caloric meal (it contains the somewhat fussy drug, rilpivirine) and cannot be taken with a PPI. At higher doses, rilpivirine rarely can affect heart function, which is unfortunate because in its current lower dose formulation it is less potent in patients with an HIV viral load greater than 100,000 copies. It therefore has earned a BI rating from DHHS and is not considered a first-line agent.

ACTIVIST BRIDGETTE PICOU SAYS: Odefsey is a good "switch" option for people who are virally suppressed (less than 50 copies) and stable on current medication regimens and also for new starts when the viral load is less than 100,000. Containing TAF makes it less kidney toxic and more bone friendly, but they should still be monitored. Be open in discussing other medications prescribed by other providers and over-the-counter medications you take to avoid potential drug-drug interactions. This is important if you take certain antacids so discuss this with your doctor or specialty pharmacist (a pharmacist certified in HIV medications is your best option next to your HIV specialist).

MANUFACTURER

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

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

AVERAGE WHOLESALE PRICE

$3,536.53/MONTH

Complera

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

STR SINGLE-TABLET REGIMEN CONTAINING AN NNRTI AND TWO NRTIs

✔ RECOMMENDED INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

One tablet once daily, with a standard meal (more than 390 calories). For people taking HIV therapy for the first time (treatment-naïve) or people with suppressed viral load on a stable HIV regimen for at least 6 months who have no known resistance to the rilpivirine, emtricitabine, or tenofovir components of the regimen. Tablet contains 25 mg of the NNRTI rilpivirine plus 200 mg emtricitabine and 300 mg tenofovir DF (TDF).

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

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

People taking HIV treatment for the first time must have an HIV RNA (viral load) of less than 100,000 copies/mL and a CD4 T cell count of more than 200 cells/mm^3 before starting Complera due to higher rates of virologic failure in these patients.

Take missed dose as soon as possible, unless it's closer to the time of your next dose. Do not double up on your next dose. Complera should not be used in people with CrCl less than 50 mL/min or severe liver impairment.

➤ **SEE THE INDIVIDUAL DRUGS CONTAINED IN COMPLERA:** Edurant and Truvada (co-formulation of Emtriva and Viread).

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Moderate to severe side effects are uncommon. Insomnia, headache, and depressive disorders (depression, negative thoughts, suicidal thoughts or actions) were each reported in 2% of study participants. Cases of rash and increased liver enzymes have also been reported with regimens containing rilpivirine. There may be a small increase in serum creatinine (SCr) and decrease in estimated creatinine clearance (CrCl) associated with rilpivirine. See Truvada page for other possible effects on kidney function. Prior to initiation, people should be tested for hepatitis B (HBV) infection. Severe exacerbations of hepatitis B have been reported in people who are co-infected with hepatitis B and have discontinued the emtricitabine and/or tenofovir components. Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted.

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POTENTIAL DRUG INTERACTIONS

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. Do not take with Epivir-HBV, Hepsera, or Vemlidy (TAF), all three used for treatment of hepatitis B. Proton pump inhibitors (PPIs, heartburn or stomach acid drugs like Aciphex, Dexilant, Nexium, Prevacid, Prilosec, Protonix, etc.) can't be taken with Complera. Antacids containing aluminum, magnesium hydroxide, or calcium carbonate can be taken at least two hours before or at least four hours after a Complera dose. Stomach acid-reducing drugs such as Pepcid, Tagamet, and Zantac can be taken at least 12 hours before or at least four hours after a Complera dose. Do not take Complera with carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifampin, rifapentine, or the herb St. John's wort (other herbals have not been studied with Complera, but consult with a pharmacist before taking any herbals or OTC supplements). Rifabutin must be taken with an extra Edurant tablet in addition to Complera. Do not take with more than one dose of the injectable steroid dexamethasone (sometimes given in the ER or hospital). Use caution if used with fluconazole, itraconazole, ketoconazole, posaconazole, and voriconazole. Use azithromycin when possible instead of the antibiotics clarithromycin, erythromycin, or telithromycin, because these drugs increase rilpivirine levels, which can increase the risk of side effects. Reduced methadone levels can occur and while dose adjustments are not necessary, it is recommended to monitor for withdrawal symptoms. Complera should also not be taken with other medications that prolong QTc interval (a heart problem) or medications with a known risk of torsades de pointes. Complera may be taken with Harvoni and Zepatier. Monitor for tenofovir toxicities with Epclusa. Not intended to be taken with other HIV medications, unless prescribed that way. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Complera can be relatively difficult to take because of its food requirement and drug interactions. In addition, strict adherence is critical due to its relatively low barrier to the development of resistance. A newer version of Complera, Odefsey, contains tenofovir alafenamide (TAF) instead of tenofovir DF; TAF is safer on kidney and bone health. Also as a result of the TAF, Odefsey can be taken by people with more advanced kidney disease, down to a renal function (CrCL) of 30 mL/min. For pregnant patients who are already on Complera prior to pregnancy and who are virologically suppressed, one tablet taken once daily may be continued. Lower exposures of rilpivirine were observed during pregnancy, therefore viral load should be monitored closely.

DR. ROSS SLOTTEN SAYS: No comment provided because it has been replaced by Odefsey.

ACTIVIST BRIDGETTE PICOU SAYS: Complera is a single-tablet regimen containing three medications. It can be used for new starts if the viral load is under 100,000, or for switching to simplify medication regimens. It is to be taken with food, and should be a meal you chew, not just a protein shake or yogurt snack. Since it does have interactions with other medications like antacids, you may want to consider the time of day you take it. Kidney and liver function should also be monitored on this medication.

MANUFACTURER

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

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

AVERAGE WHOLESALE PRICE

$3,536.53/MONTH

Atripla

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

STR SINGLE-TABLET REGIMEN CONTAINING AN NNRTI AND TWO NRTIs

✔ RECOMMENDED INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

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

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

Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. Do not split or crush the tablet. Dose cannot be adjusted for people with kidney problems and Atripla should not be used in people with moderate or severe kidney or liver impairment.

Other similar, but not exact, medications are also available (see page for Symfi and Symfi Lo, EFV/3TC/TDF).

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

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Use with caution in individuals with depression or other psychiatric issues who are not receiving mental health care. A 2014 study (reference online) reviewed four previously published AIDS Clinical Trials Group (ACTG) studies regarding efavirenz and suicidal ideation and re-emphasized the fact that efavirenz has an association with suicidality (reported suicidal ideation or attempted or completed suicide), and should be used with caution in patients with severe or uncontrolled depression and/or a history of suicidality. It is recommended for anyone on a regimen containing efavirenz to be screened for depression and suicidality. Common side effects may include dizziness, drowsiness, abnormal or vivid dreams, difficulty concentrating, rash, diarrhea, nausea, fatigue, headache, and insomnia. These side effects may go away after a few weeks. Kidney function should be assessed before initiating treatment and throughout therapy as determined by a provider. Prior to initiation, people should be tested for hepatitis B (HBV) infection. Severe exacerbations of hepatitis B have been reported in people who are co-infected with hepatitis B and have discontinued the emtricitabine and/or tenofovir components. Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted. The efavirenz component of Atripla has been associated with central nervous system (CNS) birth defects in non-human primates, and cases of neural tube defects have been reported after first trimester exposure in humans. A link between efavirenz and birth defects in humans has not been supported in meta-analyses. The recommendation is that women in their first trimester continue taking efavirenz as long as their viral load remains undetectable; however, efavirenz should only be used if the potential benefit outweighs the potential risk (as when other treatment options are not available). Because of the association with suicidality and neuropsychiatric effects, it is also recommended to screen for antenatal and postpartum depression in women with HIV who are taking a regimen containing efavirenz. The efavirenz component in Atripla can cause a false positive result for marijuana on certain drug tests. A more specific confirmatory test can be done.

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POTENTIAL DRUG INTERACTIONS

Do not take with Epivir-HBV, Hepsera, or Vemlidy (TAF), all three used for the treatment of hepatitis B. Atripla should not be taken with voriconazole, ergot derivatives, midazolam, pimozide, triazolam, bepridil, or St. John's wort. Atripla should also not be taken with other medications that prolong QTc interval (a heart problem) or medications with a known risk of torsades de pointes. No dose adjustment of Atripla needed with Sovaldi. Use caution when administering Atripla with Harvoni and monitor renal function closely due to possible increased tenofovir levels. Increase dose of Daklinza to 90 mg when used with Atripla. Atripla should not be taken with Epclusa or Zepatier. Not intended to be taken with other HIV medications, unless prescribed that way. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Atripla is listed as a "Recommended Regimen in Certain Clinical Situations" in the DHHS guidelines based on a high rate of central nervous system side effects and a possible association with suicidality. Be careful when stopping Atripla, so that you avoid the rapid development of HIV resistance to it—check with your provider or pharmacist first. Many individuals switching from Atripla to a new regimen report never realizing what a fog they had been living under.

DR. ROSS SLOTTEN SAYS: Poor Atripla, the drug that once was king! The first STR approved in 2006 (although its components, efavirenz—brand name Sustiva—and FTC/TDF, were approved a few years earlier), Atripla has fallen from Olympus. Gilead, its manufacturer, is anxious to make way for a new generation of HIV medications (especially since generic versions are appearing). No sighs or sobs for Atripla's demise. Efavirenz often causes vivid dreams and other so-called neuropsychiatric abnormalities (fatigue, depression), but many people taking it have no complaints. TDF can adversely affect kidney function and increase the risk for osteoporosis. These adverse effects were not discovered in early studies; they emerged later. Yet the drug fails to fade. I admit that I still have a good number of people on Atripla. Dr. David Hardy's statement in last year's Drug Guide that "Atripla is now rarely, if ever, used in the U.S." isn't true in my experience. When people have no side effects from a medication, they're reluctant to change to something else. "If it ain't broke, don't fix it," they'll say. Let's not forget that Atripla has saved many lives because of its potency and ease of administration. If taken at night and on an empty stomach, most people aren't bothered by the neuropsychiatric side effects. We have 20 years of experience with Atripla and the vast majority of people on it are totally fine. We have only a few years of experience with INSTIs and TAF. Let's not be so quick to bury Atripla or its generic replacements. Who knows what unknown long-term complications, if any, might arise from newer agents?

ACTIVIST BRIDGETTE PICOU SAYS: Once considered a staple and frontline treatment for HIV, Atripla is an older medicine that is still prescribed today. It has been known to have neurotoxic effects, things like fatigue, vivid dreams, and depression. Even though these side effects are known, the drug is effective and works well to control HIV when taken properly. Take it on an empty stomach and do not skip doses. Keep regular appointments with your healthcare provider to monitor liver, kidney, and central nervous system effects.

MANUFACTURER

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

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

AVERAGE WHOLESALE PRICE

$3,593.65/MONTH

Symfi and Symfi Lo

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

STR SINGLE-TABLET REGIMEN CONTAINING AN NNRTI AND TWO NRTIs

✔ RECOMMENDED INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

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

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

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

- SEE THE INDIVIDUAL DRUGS CONTAINED IN SYMFI AND SYMFI LO: Sustiva, Epivir, and Viread.
- SEE PACKAGE INSERT for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

The most common side effects occurring in 5% or more of studied individuals include headache (14%), body pain (13%), fever (8%), abdominal pain (7%), back pain (9%), asthenia (6%), diarrhea (11%), nausea (8%), vomiting (5%), arthralgia (joint pain, 5%), depression (11%), insomnia (5%), anxiety (6%), pneumonia (5%), and rash (18%). These side effects are most common at the start of treatment and usually diminish in two to four weeks. Bedtime dosing on an empty stomach can help reduce symptoms. Use with caution in individuals with depression or other psychiatric issues who are not under a psychiatrist's care. Prior to initiation, people should be tested for hepatitis B (HBV) infection.

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Severe exacerbations of hepatitis B have been reported in people who are co-infected with hepatitis B and have discontinued the lamivudine and/or tenofovir components. Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted. The efavirenz component in these medications can cause a false positive result for marijuana on certain drug tests. A more specific confirmatory test can be done.

POTENTIAL DRUG INTERACTIONS

Do not take with Epivir-HBV, Hepsera, or Vemlidy (TAF), all three used for treatment of hepatitis B. Do not take with another nephrotoxic (harmful to the kidneys) medication, such as high-dose or multiple NSAIDs (non-steroidal anti-inflammatory drugs; these include aspirin, ibuprofen – Motrin, Advil, and others, and naproxen sodium—Aleve and others). Should not be taken with voriconazole, ergot derivatives, midazolam, pimozide, triazolam, bepridil, or St. John's wort. Efavirenz should also not be taken with other medications that prolong QTc interval (a heart problem) or medications with a known risk of torsades de pointes. May affect warfarin levels. Can decrease levels of buprenorphine and methadone—monitor for withdrawal. When taken with carbamazepine, phenobarbital, or phenytoin, periodic monitoring of anticonvulsant and efavirenz levels should be done or alternative anti-seizure drugs, such as levetiracetam, should be considered. Effectiveness of birth control pills may be decreased; consider the use of other contraceptive methods. Closer monitoring and dose adjustments may be required with posaconazole (avoid unless benefit outweighs potential risk) and itraconazole. Monitor effectiveness of clarithromycin or consider using azithromycin instead. Levels of immunosuppressants should be monitored when starting or stopping Symfi or Symfi Lo. Cardizem, Lipitor, Pravachol, and Zocor doses may need to be adjusted. Titrate dose of bupropion and sertraline based on clinical response. Avoid use of sorbitol-containing medicines with lamivudine; there are many, such as acetaminophen liquid (Tylenol liquid and others). No dose adjustment of Symfi or Symfi Lo needed with Sovaldi. Use caution when administering with Harvoni and monitor renal function closely due to possible increased tenofovir levels. Should not be taken with Epclusa or Zepatier. Not intended to be taken with other HIV medications, unless prescribed that way. See Atripla page for more potential side effects. 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

Symfi and Symfi Lo are basically alternative versions of Atripla, a well-established HIV medication that's no longer preferred when starting therapy. If you can't sleep, ask your doctor about gradually adjusting the timing of your dose until it's taken during the day. A genetic trait affecting drug metabolism of Sustiva, leading to a higher rate of side effects, occurs more in African Americans. For individuals with HIV-2, commonly found in some other countries, an NNRTI would not be recommended as HIV-2 is inherently resistant to NNRTIs. GO TO aidsinfo.nih.gov.

Randomized clinical trial data have demonstrated the efficacy of lower dose (400 mg) efavirenz found in Symfi Lo along with fewer side effects. Symfi Lo is now approved in the U.S. for initial treatment of HIV infection (although guidelines no longer list it as a preferred option for someone starting medication). There is a discussion of the data on page G-31 of the guidelines.

Symfi and Symfi Lo are listed as a "Recommended Regimen in Certain Clinical Situations" in the DHHS guidelines, just as Atripla is, due to their association with a high rate of central nervous system side effects and possible association with suicidality. Be careful when stopping these medications, so that you avoid the rapid development of HIV resistance to them—check with your provider or pharmacist first.

DR. ROSS SLOTTEN SAYS: I had not heard of either of these medications until I received a notice from United Health Care in 2018 that they were among the first-tier preferences in its formulary. By switching to one of these two drugs, policyholders living with HIV would have a lower co-pay—the incentive for the switch. Not a bad idea in 2010, but not today. Symfi contains efavirenz (600 mg), lamivudine (Epivir/3TC) and tenofovir disoproxil (TDF); Symfi Lo contains a lower dose of efavirenz (400 mg), which may have fewer side effects than the higher dose, with the same nucleoside backbone as Symfi. These medications are a false choice, unless one disagrees with DHHS guidelines. If we have to switch, why not switch to Biktarvy or Triumeq? There is no longer a role for drugs like Symfi and Symfi Lo as first-line agents because we're gradually moving away from efavirenz and TDF-containing regimens in favor of agents with fewer adverse side effects.

ACTIVIST BRIDGETTE PICOU SAYS: Both Symfi and Symfi Lo are single-tablet regimens with the difference being that Symfi Lo has a lower dose of efavirenz at 400 mg vs. 600 mg in Symfi. The primary benefit of that is fewer neurologic effects like depression or insomnia. Discuss these and any history of mental concerns or upset with your doctor, as these medicines can make you feel angry or agitated under these circumstances. Rash is a common side effect that will usually go away on its own. On the plus side both Symfi and Symfi Lo cost less than comparable regimens available today.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

Symfi: **$1,961.33**/MONTH
Symfi Lo: **$1,961.33**/MONTH

INVESTIGATIONAL DRUG AT PRESS TIME

PHOTO UNAVAILABLE

cabotegravir/rilpivirine long-acting CAB LA/RPV LA

LA LONG-ACTING INJECTABLE REGIMEN; CONTAINS AN INSTI AND AN NNRTI

DHHS RECOMMENDATION NOT YET ESTABLISHED

STANDARD DOSE

Clinical trials of this investigational regimen used a long-acting cabotegravir injection of 400 mg plus 600 mg long-acting rilpivirine injection every month. There was a month-long oral lead-in using 30 mg cabotegravir plus 25 mg rilpivirine prior to initiating injections. Oral medication is also expected to be used as "bridging" if shots cannot be obtained on time. The cabotegravir tablet may not otherwise be available on the market. This regimen consists of the NNRTI rilpivirine with the new INSTI cabotegravir. Oral rilpivirine must be taken with food; the injectable does not need to be taken with food. After the month-long oral lead-in, two loading doses are administered consisting of two 3 mL injections of cabotegravir plus rilpivirine. Maintenance dose consists of two 2 mL injections of cabotegravir plus rilpivirine monthly.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

In one study, injection site reactions with mild, short-term (two to five days) redness, pain, and swelling was reported in 84% of all injections. Moderate symptoms were reported in 15% of injections. Less than 1% of patients discontinued the study due to injection site reactions. There have been rare reports of depression and suicidal ideation, primarily in patients with a history of psychiatric illnesses, in people receiving INSTI-based regimens. The DHHS guidelines recommend closely monitoring patients with pre-existing psychiatric conditions on an INSTI.

POTENTIAL DRUG INTERACTIONS

New interactions continue to be discovered after drug approval (cabotegravir is the new medication). Not intended to be taken with other HIV medications, unless prescribed that way. If used with abacavir/lamivudine during the initial oral induction phase, as this regimen was also studied, be aware of possible drug interactions with these agents (see Epzicom page). During the initial oral induction phase with rilpivirine, it is not recommended to co-administer carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifampin, rifapentine, proton pump inhibitors (Aciphex, Dexilant, Nexium, Prevacid, Prilosec, Protonix), or St. John's wort. Antacids should be taken two hours before or at least four hours after oral Edurant. Acid-reducing drugs (Pepcid, Tagamet, Zantac, and Axid) should be taken 12 hours before or 4 hours after an oral Edurant dose. Some of these interactions will no longer be relevant once injection therapy begins; however, see package insert when available for guidance. See Edurant page for more interactions. 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.

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MORE INFORMATION

There was surprise and disappointment when the FDA didn't grant approval to this drug in December 2019. Instead the FDA sent ViiV Healthcare a "complete response letter." ViiV reported that the FDA referred to "Chemistry Manufacturing and Controls," and that there were no safety issues raised by the FDA. The company said it will work with the FDA on the drug's approval. ViiV had a factory built specifically for the production of this medication, that's how different it is. In fact, this page represents a brand new category for the drug guide—a long-acting complete regimen for HIV treatment. This antiretroviral regimen is taken once a month, as two intramuscular injections. That's it. Or as ViiV Healthcare pointed out, it changes HIV treatment from 365 dosing days per year to just 12. People who are adherent to their HIV regimen now may be eligible to switch to this med when approved. The trade-off with long-acting treatment is the requirement for near-perfect adherence and visiting your doctor's office 12 times a year instead of two or three. The treatment is also one injection per butt muscle. Cabotegravir is from the top-of-the-line HIV medications right now, the INSTI drug class. They have great efficacy and are, in general, easy to take. Rilpivirine is already on the market in a variety of oral formulations (Complera, Edurant, Juluca, and Odefsey). Rilpivirine is not available separately as an injectable. Cabotegravir-LA is also being studied for HIV prevention or PrEP using one 3 mL intramuscular injection in the gluteal area every two months. The lead-in oral dosing is used to establish the safety and tolerability of cabotegravir prior to long-acting injection. For example, if an allergic reaction occurs, it can be out of the system in a day or two. In the LATTE-2 study with people on first-time HIV therapy, cabotegravir plus rilpivirine given every 4 weeks or every 8 weeks was found to be as effective as the traditional three-med (even if only as one pill) oral combination given to people in the control group of the trial. There was some virologic failure in the 8 week group vs. none in the 4 week; hence, research went forward with only 4 week dosing. This success was out to 96 weeks (nearly two years). Moreover, the majority of participants given shots in the Phase III ATLAS study (more than 96%) said they preferred the injections every month or two months to taking their previous daily HIV oral regimen, despite any side effect or injection site reaction.

DR. ROSS SLOTTEN SAYS: Cabenuva [likely name once FDA approved] is composed of the new integrase strand transfer inhibitor (INSTI) cabotegravir manufactured by GlaxoSmithKline and Janssen's NNRTI rilpivirine (Edurant). What's novel about this combination is that it is given as a once-monthly injection in the muscle (ouch!). Moreover, like Juluca, Cabenuva doesn't contain any NRTIs. In two Phase 3 studies, known as ATLAS and FLAIR, Cabenuva's efficacy matched that of Triumeq and other three-drug regimens. Patients selected for the studies had to be virally suppressed for at least six months and have no prior history of treatment failure to any regimen. Local injection site reactions were said to be mild and didn't lead to discontinuation of the medication in study subjects. In fact, the medication was otherwise very well tolerated. Presumably, Cabenuva will not be prescribed as a first-line regimen, at least initially. Patients would be switched to Cabenuva after achieving and maintaining undetectability with another anti-HIV regimen. Still, I have questions. Despite its relative convenience, will people with HIV be willing to switch to an injectable therapy? How long a grace period do they have if they don't return for treatment in 4 weeks? ViiV, the division of GSK that will be marketing Cabenuva, recently filed for FDA approval, but the FDA rejected the application not because of safety or efficacy concerns but because of incomplete information about quality control issues related to storage, distribution, and packaging information. Presumably, further investigation and clarification will lead to eventual FDA approval. Whether Cabenuva will surpass Biktarvy or Triumeq in the race to Olympus remains unclear.

ACTIVIST BRIDGETTE PICOU SAYS: This two-drug regimen will soon be an exciting new option in drug therapy. The once- or twice-monthly injectable dosing offers a freedom from taking medication daily and feeling tied to your regimen, although keep in mind that it requires a commitment to scheduling. If you are a person who splits time living between different cities seasonally, or who travels a lot, you will want to make sure you have a network in place, and that the medication is available and covered in those places. This is a deep intramuscular injection, which means it needs to be given in a doctor's office. Your tolerance for injections is also a consideration. The most common reported side effect is injection site pain, which is temporary. Even with all that, for people with adherence issues, or those who want to keep their medication routine private, this will be a fantastic alternative.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com
(877) 844-8872

AVERAGE WHOLESALE PRICE

Not yet established.

Tivicay

DTG
dolutegravir

INSTI INTEGRASE STRAND TRANSFER INHIBITOR

★ RECOMMENDED AS A COMPONENT OF INITIAL REGIMEN FOR MOST PEOPLE

STANDARD DOSE

One 50 mg tablet once daily without regard to food, for people on HIV therapy for the first time (treatment-naïve) or treatment-experienced people who have never had treatment failure with an INSTI. One 50 mg tablet twice daily, without regard to food, for people 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) which does not contain this medication or medication from the same drug class.

For adults and children weighing more than 88 pounds (40 kg). For children weighing between 35 kg (77 pounds) and 39 kg, the FDA recommends taking Tivicay 10 mg plus Tivicay 25 mg (35 mg total dose) once daily without regard to 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. 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 seen in 7% of participants in one study. Additionally, increased CPK (creatine kinase, a lab value indicating muscle damage), rhabdomyolysis (breakdown of muscle), and myopathy or myositis (muscle pain) were reported. New data associate INSTIs and TAF with weight gain; see "Weighty Concerns," beginning on page 8, and GO TO aidsinfo.nih.gov. There have been rare reports of depression and suicidal ideation, primarily in patients with a history of psychiatric illnesses, in people receiving INSTI-based regimens. The DHHS guidelines recommend closely monitoring patients on an INSTI who have pre-existing psychiatric conditions. Tivicay can cause a small, reversible increase in kidney function test (serum creatinine) within the first few weeks of treatment without affecting actual kidney function. Liver enzymes should be monitored in people with hepatitis B or C.

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POTENTIAL DRUG INTERACTIONS

Do not take with the anti-arrhythmic dofetilide. Intelence decreases Tivicay levels by 88%, therefore, these two medications must be co-administered with Kaletra, boosted Prezista, or boosted Reyataz. Tivicay should be taken two hours before or six hours after taking laxatives or antacids, the ulcer medication sucralfate, oral iron or calcium supplements, or buffered medications. It can be taken with iron- or calcium-containing supplements if taken together with food. Acid reducers (Pepcid, Zantac, Tagamet) and proton pump inhibitors (for example, Aciphex, Dexilant, Prilosec, Prevacid, Protonix, and Nexium) are okay to use. Avoid taking with Viramune, oxcarbazepine, phenytoin, phenobarbital, and St. John's wort. Start metformin at lowest dose and titrate based on glycemic control. Monitor for metformin adverse effects. Use alternatives to rifampin, carbamazepine, efavirenz, Aptivus/Norvir, and Lexiva/Norvir when possible in people with confirmed or suspected INSTI drug resistance, but these medications can be taken with Tivicay 50 mg twice daily. Should be okay to take with Epclusa, Harvoni, or Zepatier. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Tivicay (dolutegravir) is part of Juluca, Dovato, and Triumeq, all single-tablet regimens. Tivicay is considered a second-generation INSTI—it may work in many individuals whose virus has developed resistance to other INSTIs, but it needs to be dosed twice daily in these people. Compared to other INSTIs, Tivicay has a high genetic barrier against the development of resistance, similar to the protease inhibitors (such as Prezista). Tivicay has also demonstrated superiority to Prezista when looking at virologic results. Pediatric HIV guidelines added Tivicay as part of a preferred regimen. Tivicay is particularly useful when drug interactions are a concern with the HIV protease inhibitor (PI) drugs. Tivicay is a small tablet, a benefit for patients who have difficulty swallowing.

Tivicay as part of Juluca is used as a medication to switch to for people with undetectable viral loads on their current regimen for at least six months; see Juluca. Another ART (antiretroviral therapy) switch strategy with some supporting evidence for its consideration in people with viral suppression in the DHHS guidelines that uses Tivicay is switching to a boosted protease inhibitor + integrase inhibitor. In two small observational studies, individuals were switched from their current ART regimens to Prezista + Norvir + Tivicay, and viral suppression was maintained in over 97% of participants. Dolutegravir is now a preferred medication in pregnancy as well as an alternative drug for those who are trying to conceive, according to U.S. HIV perinatal treatment guidelines updated in December 2019 (GO TO aidsinfo.nih.gov/guidelines/html/3/perinatal-guidelines/0). This clears preliminary concerns over the potential for birth defects with dolutegravir raised in 2018 by a study in Botswana.

DR. ROSS SLOTTEN SAYS: Tivicay, first approved in 2013 as a single-tablet agent, is now the highest performing INSTI, either as part of an STR (Triumeq) or in combination with Descovy or Truvada. It is a very potent INSTI and has not been shown, convincingly, to have developed resistance in people who failed therapy. Interestingly, dolutegravir has been associated with weight gain in treatment-naïve patients. In an observational study conducted at the Vanderbilt University Comprehensive Care Clinic, patients taking dolutegravir experienced on average a 6 kg (13.2-pound) weight gain as opposed to patients taking elvitegravir (Genvoya) or raltegravir (Isentress). Those on elvitegravir gained 0.5 kg while those on an NNRTI gained 2.6 kg. It should be noted that this was an observational and therefore not a controlled study. Another ACTG study (A5202 and A5237) showed that those who gained weight after the initiation of HAART had higher levels of proteins associated with immune activation than those who maintained their weight so it's not clear if any medication in particular caused weight gain.

ACTIVIST BRIDGETTE PICOU SAYS: Tivicay is a tablet taken as part of an HIV cocktail with other drugs. Tivicay is potent and works well. It is dosed either once daily, or twice a day in the presence of resistance to other integrase inhibitors. Side effects may include headache, insomnia, and diarrhea.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

50 mg tablets:
$2,191.76/MONTH

Isentress HD (and Isentress) RAL raltegravir

INSTI INTEGRASE STRAND TRANSFER INHIBITOR

★ RECOMMENDED AS A COMPONENT OF INITIAL REGIMEN FOR MOST PEOPLE

STANDARD DOSE

ISENTRESS HD: **Two 600 mg film-coated tablets once daily for individuals new to HIV therapy (treatment-naïve) or who are virologically suppressed (have undetectable viral load) on an initial regimen of Isentress.**

ISENTRESS: **One 400 mg film-coated tablet twice daily for people with HIV treatment experience; this Isentress dose may also be taken by those new to HIV therapy.**

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

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

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

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

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

POTENTIAL SIDE EFFECTS AND TOXICITY

In general, raltegravir is very well tolerated with infrequent side effects. Those reported in up to 3–4% of study subjects include insomnia, nausea, and headache. The side effect profile in children is comparable to adults. New data associate INSTIs and TAF with weight gain; see "Weighty Concerns," beginning on page 8, and GO TO aidsinfo.nih.gov. Isentress may cause elevated levels of creatine kinase (a muscle enzyme). Inform your provider or pharmacist if you have a history of rhabdomyolysis, myopathy, or increased creatine kinase, or if you also take medications that may contribute to these conditions such as statins, fenofibrate, or gemfibrozil. INSTIs have been associated with adverse neuropsychiatric effects in some retrospective cohort studies and case series. The DHHS guidelines recommend closely monitoring people with pre-existing psychiatric conditions on an INSTI. Chewable tablets contain phenylalanine, which can be harmful to patients with phenylketonuria.

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POTENTIAL DRUG INTERACTIONS

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. It is important to take Isentress HD and Isentress only with other HIV drugs recommended by your provider because they and similar drugs are contained in other HIV medications: Biktarvy, Genvoya, Stribild, Tivicay, Triumeq, Dovato, and Juluca. Isentress HD cannot be used with rifampin, but Isentress can; increase Isentress to 800 mg twice daily when using rifampin. Remember to decrease the raltegravir back to its original dose when you finish taking rifampin. There are no data on dosing of the chewable tablets with rifampin. There is no need to increase the raltegravir dose with rifabutin. With both Isentress HD and Isentress, avoid Gaviscon and other antacids containing aluminum or magnesium. Calcium-containing antacids like Tums (calcium carbonate) can be used with Isentress, but not Isentress HD. Other acid reducers (such as Pepcid, Zantac, Prilosec, and Prevacid) are okay to use. Raltegravir is not recommended with carbamazepine or phenobarbital. Raltegravir can be used with Harvoni, Zepatier, or Epclusa. Unlike Isentress, Isentress HD cannot be used with Intelence or boosted Aptivus.

MORE INFORMATION

Isentress HD was approved in 2017. While the original formulation, Isentress, was well tolerated and highly effective, its twice-daily dose was seen by some as a small inconvenience. According to DHHS HIV treatment guidelines, most INSTIs on the market are recommended as components of initial ART regimens for most people; Isentress HD has been added to this list. Raltegravir-based regimens may be preferred for patients with high cardiovascular risk. Isentress is the preferred INSTI medication in HIV treatment guidelines for pregnancy, 400 mg twice a day in combination with 2 NRTIs. In pediatric HIV guidelines, Isentress was downgraded in 2017 from "preferred" to an "alternative" part of an initial regimen for children ages 6–12.

MANUFACTURER

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

DR. ROSS SLOTTEN SAYS: Isentress was the first INSTI approved in 2007. At the time of approval, it offered another potent option for patients who were resistant to other medications, like efavirenz. Initially, it was approved for twice-daily dosing. A bit too late, its manufacturer, Merck, developed a once-daily formulation, but by that time Tivicay had become available. And now there are STRs containing another INSTI, rendering Isentress a less ideal option. Nevertheless, Isentress HD has few interactions with other medications. In combination with TDF/FTC, it retains a B1 status with DHHS experts.

ACTIVIST BRIDGETTE PICOU SAYS: Isentress HD and Isentress can be used for both treatment-naïve and treatment-experienced patients, in particular those who have not taken integrase inhibitors before with multi-drug resistance. The 600 mg Isentress HD tablet is two pills taken once daily, and the 400 mg tablet is one pill twice a day. This medication is also part of the current guidelines for use in PEP (post-exposure prophylaxis) prevention regimens.

AVERAGE WHOLESALE PRICE

Isentress HD 600 mg:
$1,983.74/MONTH
Isentress 400 mg:
$1,983.74/MONTH

Prezcobix

DRV/COBI
darunavir/cobicistat

PI/PKE FIXED-DOSE COMBINATION CONTAINING A PROTEASE INHIBITOR AND A PHARMACOKINETIC ENHANCER (BOOSTER)

✔ RECOMMENDED AS A COMPONENT OF INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

One tablet (800 mg of the PI darunavir boosted by 150 mg cobicistat) once daily with food, in people with no darunavir-associated drug resistance, including both treatment-experienced individuals and those who are treatment-naïve (taking HIV therapy for the first time). Must be taken in combination with another antiretroviral(s) which does not contain the medications in this drug or medication from the same drug classes.

Prezcobix is only available for people taking darunavir once daily, not those who require darunavir twice daily (see Prezista). It is not recommended to co-administer Prezcobix with tenofovir disoproxil fumarate (brand name Viread, found in Truvada), with creatinine clearance (CrCl) less than 70 mL/min (a measure of kidney function). See "More information" for CrCL and pediatric dose update.

Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. Prezcobix is not recommended during pregnancy due to substantially lower exposures of darunavir and cobicistat during pregnancy. Do not use in people with severe liver impairment.

➤ SEE THE INDIVIDUAL DRUGS CONTAINED IN PREZCOBIX: Prezista and Tybost.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

As darunavir (contained in Prezcobix) contains a sulfa component, patients with a known sulfonamide allergy should be monitored for rash after starting it. The most common side effects reported in at least moderate severity in 5% or more of study participants were diarrhea, nausea, rash, headache, abdominal pain, and vomiting. Cobicistat can cause a small, reversible increase in serum creatinine (SCr, which indicates the eGFR or estimated CrCl lab values) within the first few weeks of treatment without affecting actual kidney function (see Tybost for more information). Patients experiencing a confirmed increase in serum creatinine of greater than 0.4 mg/dL from baseline should be closely monitored for renal safety. Serum phosphorus in patients with or at risk for kidney impairment should also be monitored. Kidney impairment, including cases of acute kidney failure and Fanconi syndrome, has been reported in patients taking both cobicistat and Viread (tenofovir DF or TDF, also found in Truvada). When used with TDF, a baseline CrCl, urine glucose, and urine protein is needed. While very rare, severe rash (in 0.4% of those taking it), accompanied in some cases by fever and/or elevations of AST/ALT (liver enzymes), can be life-threatening. Seek medical attention immediately. Observational cohort studies reported an association between some PIs (including darunavir taken with Norvir) and an increased risk of cardiovascular (CV) events. Data with darunavir plus cobicistat are too limited to make these conclusions. Although some older PIs have been associated with liver toxicity, lactic acidosis, diabetes, or fat redistribution, these conditions are only rarely, or never, observed with darunavir. With PIs, there can be increased risk for bleeding in hemophiliacs.

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POTENTIAL DRUG INTERACTIONS

Cobicistat interacts with many drugs because, as a booster, it inhibits liver enzymes involved in drug metabolism. Do not take with betamethasone, budesonide, carbamazepine, ciclesonide, dexamethasone, dronedarone, ergot derivatives, eslicarbazepine, fluticasone, triazolam, oral midazolam, lomitapide, lurasidone, methylprednisolone, mometasone, oxcarbazepine, phenobarbital, phenytoin, pimozide, rivaroxaban, Revatio, simvastatin, lovastatin, St. John's wort, triamcinolone, alfuzosin, ranolazine, or rifampin. Not recommended to be taken with avanafil, everolimus, rifapentine, salmeterol, ticagrelor, or voriconazole. Apixaban dose may need to be adjusted. 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. Do not take with colchicine if there is kidney or liver impairment. Cannot be taken with Zepatier. Based on the mechanism, drug interactions with other hepatitis C medications are probably similar to the interactions with Prezista + Norvir. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not.

MORE INFORMATION

Since Prezista (darunavir) must be used with a pharmacokinetic (PK) enhancer or booster such as cobicistat or ritonavir, this formulation makes for greater convenience, one less pill, and one less co-pay. The resulting co-formulation, however, is rather large in size, but the tablets are designed as an immediate-release formulation, so no potential problem with absorption is anticipated if the tablets are chewed, split, or crushed. A single-tablet, once-daily regimen containing darunavir/COBI/FTC/TAF is now available (see Symtuza). Darunavir is recommended as part of an initial regimen "in certain clinical situations" in DHHS guidelines. DHHS wrote this is "in part because of greater tolerability" with the integrase inhibitor medications compared to Prezista + Norvir or Prezcobix. According to the guidelines, "An example of a situation in which a darunavir-based regimen may still be preferred is when a high genetic barrier to resistance is particularly important, such as when there is substantial concern regarding a person's adherence or when antiretroviral therapy (ART) should be initiated before resistance test results are available [go to aidsinfo.nih.gov]." Examples of people needing to start treatment immediately before resistance test results are available include newly diagnosed individuals, pregnant women, and those who are experiencing certain opportunistic infections (an indication of advanced disease). In October 2019, the FDA approved a pediatric dose for Tybost (the brand name for cobicistat). The approval also allowed Tybost and Prezista to be taken by pediatric patients weighing at least 88 pounds (40 kg). (Prezista was already approved for pediatric use.) Although the Prezcobix label was not changed to note this approval, it is presumed that pediatric patients weighing at least 88 pounds can take Prezcobix. Similarly, doctors regularly prescribe Prezcobix for patients with a CrCL less than 30 and for patients on dialysis, although the label has not been updated with new data after Prezcobix came to market.

DR. ROSS SLOTTEN SAYS: For those patients on Prezista (darunavir) and Norvir (ritonavir), Prezcobix, which contains cobicistat instead of ritonavir, consolidates two medications into a single tablet. That combination was a forerunner to the once daily Symtuza but, as noted, this combination offers no advantages over other STR regimens that have few drug-to-drug interactions.

ACTIVIST BRIDGETTE PICOU SAYS: Prezcobix is a protease inhibitor that has a high barrier to resistance. The booster cobisistat means the medication can be taken once a day, but still in conjunction with other HIV meds. Keep your provider up to date on all prescribed medications including those taken over the counter, since there are drug-drug interactions to consider. The booster component of Prezcobix may affect how they work.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$2,421.84/MONTH

Prezista DRV darunavir

PI PROTEASE INHIBITOR

✔ RECOMMENDED AS A COMPONENT OF INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

One 800 mg tablet with 100 mg Norvir or 150 mg Tybost once daily with food for treatment-naïve people (those taking HIV therapy for the first time) and treatment-experienced adults without Prezista-related resistance. One 600 mg tablet with 100 mg Norvir twice daily with food for pregnant women and those who have at least one Prezista-related resistance mutation. Prezista should always be taken with Norvir or Tybost. Must also be taken in combination with another antiretroviral(s) which does not contain this medication or medication from the same drug class.

For adults and children 3 years of age and older weighing at least 22 pounds (10 kg). Prezista for children is dosed based on weight. There are 75 mg and 150 mg tablets as well as an oral suspension (100 mg/mL) (strawberry cream flavor) available for children three and older and adults who can't swallow pills.

Suspension needs to be taken with Norvir or Tybost, with food.

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

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Prezista contains a sulfa component and should be used with caution in patients with severe sulfa allergies. Most common side effects may include diarrhea, nausea, headache, rash, vomiting, and abdominal pain. Measure liver function before starting and then monitor, with perhaps closer monitoring for those with underlying liver problems, especially during the first several months. No dose adjustment necessary with mild to moderate liver disease, but Prezista + Norvir is not recommended for those with severe liver impairment. While very rare, severe rash (in 0.4% of those taking it), accompanied in some cases by fever and/or elevations of AST/ALT (liver enzymes), can be life-threatening. Seek medical attention immediately.

When used with Tybost a small increase in serum creatinine (SCr) may be seen which does not translate to a decrease in kidney function. Observational cohort studies reported an association between some PIs (including darunavir) and an increased risk of cardiovascular (CV) events. Although some older PIs have been associated with liver toxicity, lactic acidosis, diabetes, or fat redistribution, these conditions are only rarely, or never, observed with darunavir. IRIS (immune reconstitution inflammatory syndrome) may occur as the immune system regains strength; signs and symptoms from previous infections may occur soon after HIV treatment is initiated. Report symptoms of illness, such as shingles or TB, to a health care provider. Protease inhibitors can cause increased risk for bleeding in hemophiliacs.

POTENTIAL DRUG INTERACTIONS

Drug interactions of Prezista + Norvir may be different than those for Prezista + Tybost. Of note, Tybost is not interchangeable with Norvir. Do not take with alfuzosin, cisapride, colchicine (in patients with kidney or liver impairment), dronedarone, ivabradine, lomitapide, lurasidone, naloxegol, ranolazine, pimozide, ergot derivatives, triazolam, oral midazolam, rifampin, Revatio, Xarelto, or St. John's wort. Not recommended to be taken with everolimus and ticagrelor. Tramadol dose decrease may be needed. Monitor therapeutic effects and adverse reactions with use of some analgesics, such as fentanyl and oxycodone. Monitoring of clonazepam is recommended. Reduced dose of rifabutin is recommended. Do not use lovastatin or simvastatin, or co-formulations containing these drugs (Advicor and Vytorin). Cholesterol-lowering alternatives are rosuvastatin, atorvastatin (should not exceed 20 mg per day), pitavastatin, and pravastatin, but should be used with caution and started at the lowest dose possible. Monitor for increased side effects from these medications. Reduce clarithromycin dose by 50 to 70% in kidney impairment. The antifungal drugs itraconazole or ketoconazole should be used with caution (maximum dose is 200 mg per day for either). Voriconazole should not be used unless the benefits outweigh the risks. Prezista increases levels of nasal and inhaled fluticasone (found in Advair, Flonase, Breo Ellipta, Arnuity Ellipta, and Flovent) and budesonide, as well as systemic corticosteroids ciclesonide, betamethasone, dexamethasone, methylprednisolone, mometasone, and triamcinolone. Use alternative corticosteroid and monitor for signs of Cushing's syndrome. Beclomethasone, prednisolone, and prednisone as alternative corticosteriods may be considered, particularly for long-term use. Effectiveness of oral contraceptives may be decreased; consider using alternative methods of contraception. Monitoring is recommended with methadone. Titration or decreased dose may be needed for buspirone, diazepam, estazolam, and zolpidem. Therapeutic drug monitoring is recommended for antiarrhythmics amiodarone, bepridil, disopyramide, flecainamide, systemic lidocaine, mexiletine, propafenome, 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. ROSS SLOTTEN SAYS: First approved in 2006, Prezista has become the preferred PI because of its relative lower side effect profile, although GI symptoms like diarrhea remain a problem for that class of medications. Prezista has replaced Kaletra as the preferred PI. In treatment-naïve individuals, its 800 mg formulation can be taken once daily. For those individuals with underlying resistance to other PIs, Prezista should be taken twice daily in its 600 mg formulation in combination with other medications.

ACTIVIST BRIDGETTE PICOU SAYS: Prezista is considered a lipid-friendly drug. The action of certain medications may be increased or decreased because the metabolism of the booster component of a Prezista-based regimen takes place in the liver. Talk to your provider about all medications you take. Side effects can include nausea, diarrhea, and rash.

MORE INFORMATION

Prezista, which is found in the single-tablet regimen Symtuza (see that page), is recommended as part of an initial regimen "in certain clinical situations" in DHHS guidelines. DHHS wrote this is "in part because of greater tolerability" with the integrase inhibitor medications compared to Prezista + Norvir or Prezcobix. There is growing evidence that a protease inhibitor-based regimen, boosted by ritonavir plus Epivir (lamivudine), can maintain viral suppression in patients who initiated triple-drug therapy, who achieved sustained viral suppression for at least 1 year, and who have no evidence of, or risk of resistance to, either darunavir or lamivudine. Use of Prezista with Norvir and Epivir may be a reasonable option when the continued use of TDF, TAF, or ABC is contraindicated or not desirable. Additionally, another ART switch strategy with some supporting evidence in patients with viral suppression in the DHHS guidelines is to switch patients to a boosted protease inhibitor + integrase inhibitor. In two small observational studies, patients were switched from their current ART regimens to Prezista + Norvir + Tivicay, and viral suppression was maintained in over 97% of participants. For patients on a complicated salvage regimen with current viral suppression and a history of treatment failure, there is evidence to support simplifying the regimen to a combination of Genvoya + Prezista. Prezista + Norvir is a preferred component in the DHHS perinatal guidelines for use in pregnancy. Prezista + Tybost is also found in the fixed-dose tablet Prezcobix.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

800 mg tablets:
$2,118.88/MONTH

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Evotaz

ATV/COBI
atazanavir/cobicistat

PI/PKE FIXED-DOSE COMBINATION CONTAINING A PROTEASE INHIBITOR AND A PHARMACOKINETIC ENHANCER (BOOSTER)

✔ RECOMMENDED AS A COMPONENT OF INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

One tablet once daily with food. Each tablet contains 300 mg of atazanavir boosted by 150 mg cobicistat. Must be taken in combination with another antiretroviral(s) which does not contain the medications in this drug or medication from the same drug classes. Use with Intelence or Sustiva is not recommended. See "More information" for pediatric dose update.

Use in treatment-experienced patients depends on protease inhibitor drug resistance. Co-administration with drugs containing tenofovir disoproxil fumarate (Viread, found in Atripla, Cimduo, Complera, Delstrigo, Stribild, Symfi, Symfi Lo, Temixys, and Truvada) is not recommended if kidney function as measured by creatinine clearance is below 70 mL/min. Co-administration with drugs containing tenofovir alafenamide (Vemlidy, found in Biktarvy, Descovy, Genvoya, Odefsey, and Symtuza) is not recommended if kidney function as measured by creatinine clearance is below 30 mL/min.

Not recommended in people with any degree of liver impairment or those who are treatment-experienced and on hemodialysis.

Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. Evotaz is not recommended during pregnancy due to substantially lower exposures of atazanavir and cobicistat during pregnancy.

➤ SEE THE INDIVIDUAL DRUGS CONTAINED IN EVOTAZ: Reyataz and Tybost.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

The most common (greater than 10%) side effects reported in clinical trials were nausea, ocular icterus (yellowing of the eyes), and jaundice. Rash has also been reported, though less common. Cobicistat can cause a small, reversible increase in serum creatinine (SCr, which indicates the eGFR or estimated CrCl lab values) within the first few weeks of treatment without affecting actual kidney function (see Tybost for more information). Patients experiencing a confirmed increase in serum creatinine of greater than 0.4 mg/dL from baseline should be closely monitored for renal safety. Serum phosphorus in patients with or at risk for kidney impairment should also be monitored. Kidney impairment, including cases of acute kidney failure and Fanconi syndrome, has been reported in patients taking both cobicistat and Viread (tenofovir DF or TDF, also found in Truvada). When used with TDF, a baseline CrCl, urine glucose, and urine protein is needed; CrCl, urine glucose, and urine protein should be monitored regularly while taking Tybost-containing regimens. Observational cohort studies reported an association between some PIs (including darunavir, found in Prezista and Prezcobix, and lopinavir/ritonavir, brand name Kaletra) and an increased risk of cardiovascular (CV) events; however, this has not been observed with Reyataz (atazanavir, or ATV), found in Evotaz. Another observational cohort study of predominantly male participants found a lower rate of cardiovascular events in those receiving atazanavir-containing regimens compared with other regimens. Further study is needed.

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POTENTIAL DRUG INTERACTIONS

Cobicistat interacts with many drugs, because as a booster it inhibits liver enzymes involved in drug metabolism. Of note, Tybost is not interchangeable with Norvir. Do not take with ergot derivatives, triazolam, oral midazolam, lurasidone, pimozide, Revatio, simvastatin, lovastatin, St. John's wort, Viramune, alfuzosin, ranolazine, rifampin, dronedarone, or irinotecan. Do not take with colchicine if there is kidney or liver impairment. Proton pump inhibitors (PPIs, like Aciphex, Dexilant, Nexium, Protonix, and Prevacid) and H2-receptor antagonists (H2RAs, like Pepcid, Zantac, and Tagamet) can stop atazanvir from being absorbed. Treatment-experienced people should not take PPIs while on atazanvir. See package insert for antacid dose adjustment. If taking chewable antacids like Rolaids and Tums, take atazanavir with food two hours before or one hour after. Monitoring is required when used with warfarin. Calcium channel blockers should be monitored. Reducing dose and frequency of rifabutin to 150 mg every other day or three times a week is recommended. Evotaz increases levels of fluticasone (found in Advair, Flonase, and Flovent); monitor for signs of Cushing's syndrome. An alternative corticosteroid is recommended. ED 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 use with Olysio, Viekira Pak, or Zepatier. Can be used with Sovaldi, Daklinza (reduce Daklinza dose to 30 mg), or Harvoni (if TDF is not part of the HIV regimen). Monitor for tenofovir toxicities with Epclusa if TDF is part of the regimen. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

DR. ROSS SLOTTEN SAYS: Evotaz is a combination formulation containing the PI atazanavir and the boosting agent cobicistat. It's not clear where this medication fits in today, except for individuals who were taking atazanavir with ritonavir. Although atazanavir is a potent antiretroviral agent, its side effect of jaundice in some individuals makes it a less desirable option. The jaundice is not a sign of liver disease, but it's an unpleasant side effect. Atazanavir and TDF/FTC are categorized as B1 by the panel of experts at the DHHS, but the combination is likely to further fall out of favor with the passage of time.

ACTIVIST BRIDGETTE PICOU SAYS: Two drugs combined in a single tablet (atazanavir and cobicistat), Evotaz is indicated for both treatment-naïve and treatment-experienced individuals. It should be taken with other HIV medicines. The booster means monitoring for drug-drug interactions. Like some other HIV medications, if you have heartburn and use antacids, discuss appropriate time spacing in between taking your HIV medication and the antacids as they interfere with how the atazanavir is absorbed. You may notice yellowing of the eyes and skin. This is due to an increase in bilirubin. It's harmless, but should be reported to your healthcare provider.

MORE INFORMATION

Evotaz is an alternative PI for first-time therapy in DHHS HIV treatment guidelines, and is one of two PIs that are co-formulated with the booster cobicistat (the other is Prezcobix). Since most people who take Reyataz must use it with a PK enhancer like cobicistat (Tybost) or ritonavir (Norvir), this formulation makes for greater convenience, one less pill, and one less co-pay. Tybost is not an HIV medication. Similar to ritonavir, it is used to boost blood levels of other drugs. The two PK enhancers have a long list of drug interactions. Maintaining adequate hydration is important with Evotaz. Reyataz + Tybost + Epzicom is no longer included in the list of "Recommended Initial Regimens in Certain Clinical Situations" because it has disadvantages when compared with other regimens in this category. In October 2019, the FDA approved a pediatric dose for Tybost (the brand name for cobicistat). The approval also allowed Tybost and Reyataz to be taken by pediatric patients weighing at least 77 pounds (35 kg). (Reyataz was already approved for pediatric use.) Although the Evotaz label was not changed to note this approval, it is presumed that pediatric patients weighing at least 77 pounds can take Evotaz.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$1,926.56/MONTH

GENERIC IS AVAILABLE.

Reyataz

atazanavir, or ATV
atazanavir sulfate

PI PROTEASE INHIBITOR

✔ RECOMMENDED AS A COMPONENT OF INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

For most treatment-naïve (first time on HIV therapy) and treatment-experienced individuals, the dose is one 300 mg capsule plus 100 mg Norvir or 150 mg Tybost once daily with food. Must be taken in combination with another antiretroviral(s) which does not contain this drug or medication from the same drug class. See package insert for dosing recommendations during pregnancy, liver or kidney impairment, and with certain drug interactions. Capsules also available in 150 mg and 200 mg. Take Norvir or Tybost at same time as Reyataz. Pediatric dose with 50 mg oral powder available based on body weight for children at least 3 months of age weighing at least 11 pounds (5 kg).

Take missed dose as soon as possible, unless it's closer to the time of your next dose. Do not double up on your next dose. Swallow capsules whole—do not open or mix with anything. Oral powder may be used by adult patients who cannot swallow the capsules.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Most common side effects may include nausea, ocular icterus (yellowing of the skin or eyes as a result of increased bilirubin levels), jaundice, and rash. The ocular icterus and jaundice were reversible on discontinuation of the drug. Other less common side effects may include kidney stones, gallstones, abnormal heart rhythm, and elevated liver enzymes (more common in people with hepatitis B or C). Capsules do not contain phenylalanine but oral powder does; thus, use with caution in individuals with phenylketonuria (PKU). Kidney laboratory testing should be performed in all patients prior to initiation of Reyataz and continued during treatment. Renal laboratory testing should include serum creatinine, estimated creatinine clearance, and urinalysis with microscopic examination. Rarely, chronic kidney disease has been observed.

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Observational cohort studies reported an association between some PIs (including darunavir, found in Prezista and Prezcobix, and lopinavir/ritonavir, brand name Kaletra) and an increased risk of cardiovascular (CV) events; however, this has not been observed with Reyataz (atazanavir, or ATV). Another observational cohort study of predominantly male participants found a lower rate of cardiovascular events in those receiving atazanavir-containing regimens compared with other regimens. Further study is needed.

POTENTIAL DRUG INTERACTIONS

Do not use with alfuzosin, rifampin, irinotecan, ergot derivatives, triazolam, oral midazolam, St. John's wort, Revatio, or Viramune (nevirapine). Do not use lovastatin, simvastatin, or co-formulations containing them (Advicor and Vytorin) for treatment of high cholesterol. Alternatives for these are atorvastatin, rosuvastatin, pravastatin, pitavastatin, and fluvastatin, but should be used with caution and started at the lowest dose possible; monitor for increased side effects. Of note, 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 Reyataz. See package insert for antacid dose adjustment. If taking chewable antacids like Rolaids and Tums, take Reyataz with food two hours before or one hour after. Treatment-experienced people should not take Reyataz with Sustiva. Viread decreases the levels of Reyataz and Reyataz/Norvir increases Viread levels; monitor for adverse events. Reyataz can be taken unboosted with Epzicom if absolutely necessary. Bepridil, amiodarone, quinidine, and lidocaine should be used cautiously because of the risk of worsening abnormal heart rhythm. Close monitoring is required when used with warfarin. Calcium channel blockers should be monitored. Use caution when using the antifungals itraconazole or ketoconazole. Voriconazole is not recommended. Reducing dose and frequency of rifabutin to 150 mg every other day or three times a week is recommended. Reyataz + Norvir increases levels of fluticasone (found in Advair, Flonase, and Flovent); monitor for signs of Cushing's syndrome. An alternative corticosteroid is recommended. Reyataz can be taken with birth control pills that contain no more than 30 mcg of ethinyl estradiol if taking Reyataz without Norvir and at least 35 mcg if taken with Norvir. Use caution with carbamazepine, phenobarbital, and phenytoin. ED drugs should not exceed 10 mg Cialis or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours. A lower dose of trazodone is recommended. Use with caution with bosentan, salmeterol, and immunosuppressants, and use lower dose of colchicine. Use with Norvir when taking buprenorphine; monitor for sedation. Do not take with Zepatier. Reyataz/Norvir is not recommended with Harvoni if tenofovir DF (TDF, in Truvada) is part of HIV regimen. With Epclusa, monitor for tenofovir toxicities if TDF is part of 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.

DR. ROSS SLOTTEN SAYS: Reyataz or atazanavir was first approved in 2003 as an alternative PI to Kaletra because of ease of administration and better tolerance. It can be given with or without a booster, although without a booster, there is greater risk of resistance. However, Reyataz was eventually eclipsed by Prezista in part because it causes jaundice in 10 percent of patients. I don't mean just yellow eyes; I mean quite striking yellow skin like someone with acute hepatitis, although the rise in bilirubin—the cause of the jaundice—is not due to liver impairment. Like its forebear Crixivan (indinavir), it can crystalize in the kidneys and cause kidney stones, another unpleasant adverse effect. Despite a B1 rating by the DHHS expert panel when combined with TDF/FTC, what role boosted atazanavir will have in the future is unclear. It is likely to follow Kaletra to the pharmaceutical graveyard.

ACTIVIST BRIDGETTE PICOU SAYS: Reyataz, or atazanavir, is taken with other HIV medications and is a lipid-friendly protease inhibitor. Atazanavir may cause an increase in bilirubin, which can cause your eyes or skin to appear yellow. This a harmless side effect and usually disappears after stopping the medication. Know that you should talk about use of acid reflux medication with your doctor as these may prevent full absorption of Reyataz.

MORE INFORMATION

Yellowing of the eyes and skin is a common reason for discontinuation. Reyataz plus Norvir and 2 NRTIs is still recommended as a preferred regimen during pregnancy. Reyataz plus Tybost (Evotaz) is not recommended during pregnancy. Maintaining adequate hydration is important with Reyataz. Reyataz + Norvir + Epzicom is no longer included in the list of "Recommended Initial Regimens in Certain Clinical Situations" because it has disadvantages when compared with other regimens in this category.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

300 mg, 30 capsules:
$1,739.30/MONTH
Generic atazanavir
300 mg, 30 capsules:
$1,652.33/MONTH

GENERIC IS AVAILABLE.

Norvir

RTV
ritonavir

PKE PHARMACOKINETIC ENHANCER (BOOSTER); ALSO AN ANTIRETROVIRAL (PROTEASE INHIBITOR)

✔ USED ONLY ONLY AS A BOOSTER FOR OTHER DRUGS; RECOMMENDED AS A COMPONENT OF INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

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

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

Approved for children older than one month with dosing based on body surface area; the use in children depends on the co-administered PI. Capsule formulation requires refrigeration, but tablet does not. Liquid formulation available (80 mg/mL) in peppermint caramel flavor, but is not very palatable. The taste of the liquid can be improved by mixing with chocolate milk, peanut butter, Ensure, or Advera within one hour of dosing. The liquid formulation should not be taken by pregnant women, as it contains 43% alcohol. Norvir oral powder available in 100 mg packets, is free of alcohol and propylene glycol (both of which are found in the liquid formulation), and thus safer for pediatric use.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

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

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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, 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. Norvir use 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 4 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 2–3-fold increase in methamphetamine concentrations and puts user at 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 other drug interactions which are not listed here.

DR. ROSS SLOTTEN SAYS: The only reason to mention the protease inhibitor Norvir (ritonavir) is that its primary role today is as a boosting agent for other PIs like darunavir and atazanavir. It is no longer used as an agent to treat HIV (too large a pill burden when first approved in 1996). However, it is gradually being replaced by cobicistat, another boosting agent that can be combined into a single-tablet regimen with other agents. Because cobicistat has no anti-HIV activity, unlike ritonavir, there is no potential for inducing resistance to PIs.

ACTIVIST BRIDGETTE PICOU SAYS: Norvir is used as a booster in conjunction with protease inhibitors (PIs). It should not be taken alone. Although originally marketed for use as a PI treatment for HIV, the fact that it had disabling side effects on the gastrointestinal system and toxicity on the liver made it hard to tolerate long term. It was found however that at a lower dose and as a booster it could be used successfully with newer generation protease inhibitors. Norvir may increase the effects of some medications, including those taken over the counter, so discuss these with your doctor.

MORE INFORMATION

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

COBI
cobicistat

PKE PHARMACOKINETIC ENHANCER (BOOSTER); NOT AN ANTIRETROVIRAL

✔ USED ONLY AS A BOOSTER FOR OTHER DRUGS; RECOMMENDED AS A COMPONENT OF INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

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 and Genvoya.

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; darunavir patients must be at least three years old)). Tybost is not an HIV drug; it is a pharmacokinetic enhancer or a "booster" used to increase the levels of Prezista 800 mg once daily, Reyataz 300 mg once daily, or elvitegravir 150 mg in Stribild and Genvoya. Tybost is not interchangeable with Norvir when used to increase the levels of other HIV medications.

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

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Side effects observed in clinical studies (greater than 2% of patients) include rash, jaundice, and yellowing of the eyes. However, it was studied with Reyataz so the jaundice and yellowing of eyes were most likely due to the Reyataz component. Before taking Tybost, kidney function testing should be conducted, including serum creatinine, serum phosphorus, urine glucose, and urine protein. These measurements should continue to be monitored while taking Tybost. Cobicistat can cause a small, reversible increase in serum creatinine within the first few weeks of treatment without affecting actual kidney function. The SCr increase occurred within weeks of starting cobicistat and was reversible within a few days after stopping it. The co-adminstration of Tybost and Viread (tenofovir DF or TDF, also found in Complera, Delstrigo, Symfi/Symfi Lo, Stribild, Truvada, and Temixys) is not recommended if the CrCl is less than 70 mL/min.

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POTENTIAL DRUG INTERACTIONS

Tybost interacts with many drugs. Do not take with alfuzosin, colchicine, dihydroergotamine, dronedarone, ergotamine, irinotecan, simvastatin, lovastatin, lurasidone, methyl-ergonovine, ranolazine, rifampin, pimozide, triazolam, oral midazolam, Revatio, or St. John's wort. Tybost may increase levels of nasal or inhaled fluticasone (Flonase, Advair, Breo Ellipta, Arnuity Ellipta, and Flovent). Use an alternative corticosteroid and monitor for signs of Cushing's syndrome (increased abdominal fat, fatty hump between the shoulders, rounded face, red/purple stretch marks, 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. Do not take with Olysio, Viekira Pak, or Zepatier. Avoid Harvoni if tenofovir disoproxil fumarate (TDF) is part of the HIV regimen. Tybost has similar drug interactions as Norvir, but they are not interchangeable and there may be some drug interactions with Tybost that are not observed with Norvir. Tybost may increase levels of methamphetamines. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

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

DR. ROSS SLOTTEN SAYS: Tybost was originally developed as a booster for the integrase inhibitor elvitegravir (see Stribild and Genvoya). In a head-to-head comparison of Reyataz (plus 2 NRTIs) boosted with Tybost or Norvir, no significant differences in effectiveness or side effects between the two boosters was seen. In fact, on a molecular basis, the two drugs are almost identical. A few small molecular changes in Tybost have taken away its anti-HIV activity, so it is not considered an antiretroviral, unlike Norvir. Tybost has fewer unwanted drug-drug interactions compared to Norvir

ACTIVIST BRIDGETTE PICOU SAYS: Used to "boost" the effectiveness of HIV meds, Tybost (cobisistat) is a pharmacokinetic enhancer. In other words, it makes antiretroviral (ARV) medications work better, but is not an ARV itself. Its mechanism of action in the liver means it does have the potential to create drug-drug interactions with certain other medications, so monitor for these with your doctor. You should also have regular monitoring of your lipids and triglycerides.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$290.08/MONTH

Descovy

FTC/TAF
emtricitabine/tenofovir alafenamide

NRTI — FIXED-DOSE COMBINATION OF TWO NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NUCLEOSIDE, OR "NUKE")

★ RECOMMENDED AS A COMPONENT OF INITIAL REGIMEN FOR MOST PEOPLE

STANDARD DOSE

One tablet once daily, without regard to food. Tablet contains 200 mg emtricitabine and 25 mg tenofovir alafenamide. For adults and children weighing at least 55 pounds (25 kg), or 77 pounds (35 kg) if taking Descovy with a boosted protease inhibitor. Crushing or splitting tablets has not been studied and is not recommended; TAF is soluble in water, but has a bitter and burnt aromatic flavor profile. Must be taken in combination with another antiretroviral(s) which does not contain the medications in this drug combination.

Take a missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. Descovy should not be used if CrCl is less than 30 mL/min, but can be used if CrCl is less than 15 mL/min if you are on dialysis. 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 (but TAF is not available separately for HIV).
- 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 may experience nausea, headache, stomach pain, or changes in weight. New data associate INSTIs and TAF with weight gain; see article on page 8 and GO TO aidsinfo.nih.gov. Skin discoloration on palms and soles may also occur. May affect the bones and kidneys. In clinical trials, fewer bone and kidney issues were observed with the TAF formulation compared to the TDF formulation. Tell your provider about any pain in extremities, persistent or worsening bone pain and fractures, with or without muscular pain or weakness, as well as any concerning changes in urinary habits as these could be signs of kidney problems. If you have HIV and HBV, guidelines recommend treatment for both viruses. Descovy can be used to treat HIV and HBV simultaneously. If you are co-infected with HBV and HIV, you should not stop Descovy without medical supervision because it can cause your HBV to flare and cause you to experience signs and symptoms of acute hepatitis. HBV should be closely monitored by your provider.

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POTENTIAL DRUG INTERACTIONS

Do not take with Epivir-HBV, Hepsera, 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 like Advil or Motrin (ibuprofen) and Aleve (naproxen). Descovy should not be taken with certain anticonvulsants (including carbamazepine, oxcarbazepine, phenobarbital, and phenytoin), Aptivus/Norvir, rifabutin, rifampin, rifapentine, or St. John's wort. Can be used with hepatitis C drugs such as Epclusa, Harvoni, or Zepatier. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Descovy is the newer version of Truvada. Instead of TDF, Descovy contains TAF (tenofovir alafenamide), which reduces serum tenofovir concentration by up to 90%. This results in a decreased impact on kidney and bone demineralization but maintains potent antiviral activity in the CD4 cell. In clinical trials, fewer kidney and bone issues were observed with TAF than with TDF, and significant improvements were observed when switching from TDF to TAF. The long-term impact of TAF on patients with osteopenia or osteoporosis is unknown. Both Descovy and Truvada are currently recommended by DHHS HIV treatment guidelines for first-time therapy for most people. Descovy received FDA approval in October 2019 for the prevention of sexually acquired HIV (pre-exposure prophylaxis, or PrEP) in adults and adolescents weighing at least 77 pounds, excluding individuals at risk from receptive vaginal sex, due to a lack of efficacy data in this population. It was studied in men who have sex with men and transgender women. See Descovy for PrEP page. Because both FTC and TAF are also active against hepatitis B (HBV), Descovy is recommended by DHHS for individuals co-infected with both HIV and hepatitis B. Pediatric HIV guidelines added Descovy last year as part of a preferred regimen. There is insufficient data in pregnancy for the DHHS to recommend the routine use of Descovy in pregnant women at this time. Descovy tablets are relatively small compared to Truvada and other combination tablets, which may be a plus for patients who have difficulty swallowing.

MANUFACTURER

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

DR. ROSS SLOTTEN SAYS: Approved in 2016 as a version of Truvada with a better safety profile (it contains TAF instead of TDF), Descovy has replaced Truvada as the A1 nucleoside backbone for most antiretroviral treatment regimens today. It can be combined into a single tablet regimen (Genvoya, Biktarvy, Odefsey, and Symtuza) or prescribed as part of a two-tablet regimen with other PIs, NNRTIs and INSTIs. In October 2019, the FDA approved its use for PrEP (pre-exposure prophylaxis) after clinical trials demonstrated its equivalence to Truvada in preventing HIV infection. Because the risk of harmful effects on the kidney and bone density are significantly lower, Descovy no doubt will replace Truvada for PrEP.

ACTIVIST BRIDGETTE PICOU SAYS: Descovy is the newer version of Truvada. It is thought to be safer than the old formulation because of the change to the component tenofovir alafenamide fumarate, also called TAF, instead of the tenofovir disoproxil fumerate (TDF). With fewer bone and kidney effects, TAF is popular and already being used in several of the new single-tablet regimens. Descovy has also recently been approved for PrEP (see Descovy for PrEP page in this guide). It is also considered front line treatment as part of an HIV cocktail. There are some drug interactions to consider, and while blood and kidney effects are reduced, there is still a need to monitor. Discuss medications you take with your doctor and have your labs done consistently.

AVERAGE WHOLESALE PRICE

$2,210.74/MONTH

APPROVED AS GENERIC, WHICH IS NOT YET COMMERCIALLY AVAILABLE IN THE U.S.

Truvada

FTC/TDF
emtricitabine/tenofovir DF

NRTI FIXED-DOSE COMBINATION OF TWO NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NUCLEOSIDE, OR "NUKE")

★ RECOMMENDED AS A COMPONENT OF INITIAL REGIMEN FOR MOST PEOPLE

STANDARD DOSE

One tablet once daily without regard to food for adults and children weighing at least 77 pounds (35 kg). In children weighing 37–76 pounds (17–34 kg), Truvada is dosed based on body weight. See package insert for weight-based dosing. Truvada tablets are available in the following emtricitabine/tenofovir DF dosages: 100/150 mg tablets, 133/200 mg tablets, 167/250 mg tablets, and 200/300 mg tablets. Tablets can disintegrate in water, grape juice, or orange juice with minor stirring and pressure from a spoon; however, no studies have been performed to evaluate the pharmacokinetics (PK) or stability of crushed vs. intact tablets. Must be taken in combination with another antiretroviral(s) which does not contain the medications in this drug combination.

Take a missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. The dosing frequency needs to be adjusted for people with decreased kidney function. The dose of Truvada should be adjusted if CrCl is less than 50 mL/min and Truvada should not be used if CrCl is less than 30 mL/min (less than 60 mL/min if used for PrEP) or if you are on dialysis.

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

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

POTENTIAL DRUG INTERACTIONS

Overall, Truvada is well tolerated, but some may experience nausea, headache, bloating, stomach pain, or weight loss. Rare skin discoloration on palms and soles may also occur. The TDF in Truvada is associated with long-term decreases in bone mineral density (BMD). BMD monitoring should be considered in people who have a history of bone fracture due to disease or are at risk for osteopenia or osteoporosis. While calcium and vitamin D levels can be checked to assess the need for these supplements, talk with your provider before starting on your own. Truvada can cause kidney toxicities.

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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. Routine monitoring of estimated creatinine clearance, serum phosphorus, urine glucose, and urine protein should be performed in all individuals with mild kidney impairment. If you have HIV and HBV, guidelines recommend treatment for both viruses. Truvada can be used to treat HIV and HBV simultaneously. If you are co-infected with HBV and HIV, you should not stop Truvada without medical supervision because it can cause your HBV to flare and cause you to experience signs and symptoms of acute hepatitis. HBV should be closely monitored by your provider. Truvada is associated with lower lipid levels than Ziagen or tenofovir AF (TAF) due to tenofovir DF's favorable effect on LDL (bad) cholesterol (although it also lowers levels of HDL, or good cholesterol). The ratio of total cholesterol to HDL remains the same as that of tenofovir AF. Truvada contains lactose, which can cause some abdominal discomfort, especially in patients sensitive to lactose.

POTENTIAL DRUG INTERACTIONS

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

MORE INFORMATION

Don't believe the hucksters: Truvada is a safe medication to take. As with any drug therapy, some people will experience side effects. Adverse events are rare and usually reversible. SEE "Truvada Safety" in the September+October 2019 issue of POSITIVELY AWARE (positivelyaware.com/articles/truvada-safety). Current DHHS HIV treatment guidelines recommend Truvada (or Descovy) over Epzicom as the preferred NRTI component for initial therapy (unless Epzicom is paired with Tivicay). The newer version of Truvada, called Descovy, was approved in 2016. The ACTG A5202 study reported that while both Epzicom and Truvada reduced viral load, for those people who started treatment with a viral load of more than 100,000 copies/mL, the times to virologic failure and the first adverse event were both significantly shorter in patients taking Epzicom compared to Truvada. In studies using Tivicay in the regimen, however, Truvada and Epzicom were equally effective regardless of baseline viral load. Kidney function must be monitored before and during treatment with Truvada and it may not be a good option for patients with underlying kidney problems. Fewer kidney and bone issues were observed with the TAF formulation compared to TDF in clinical trials. Truvada was approved in 2012 for HIV prevention (pre-exposure prophylaxis, or PrEP) in confirmed HIV-negative adults; see Truvada for PrEP page. In October 2019, Descovy also received FDA approval as PrEP for sexually-acquired HIV for adults and adolescents weighing at least 77 pounds, excluding individuals at risk from receptive vaginal sex; see Descovy for PrEP page. Truvada is recommended by DHHS as one of the preferred NRTI combination components of an ART regimen in pregnancy.

DR. ROSS SLOTTEN SAYS: Truvada was approved in 2004 (on the same day as Epzicom, see that page) as a two-drugs-in-one-pill, two-nuke combination "backbone" to which a third drug is added to create a three-drug combination or "cocktail" ART regimen. Truvada was the most commonly prescribed antiretroviral for the majority of PLWH from the late 2000s until Descovy was approved in 2016. This was due to Truvada's solid track record as a potent, well-tolerated, and durable two-nuke combination, data showing its higher potency over Epzicom, and concerns (still controversial) about Epzicom's cardiovascular side effects. Truvada's use has steadily declined since the approval of four TAF-containing medications (Biktarvy, Genvoya, Odefsey, and Descovy) due to less long-term side effects (kidney and bone strength). Truvada became the first medication approved for pre-exposure prevention (PrEP) of HIV in 2012. In mid-December 2017, a generic form of Truvada was approved in the U.S. With the availability of TAF-containing medications, the use of generic Truvada, while probably less expensive, has yet to be seen.

ACTIVIST BRIDGETTE PICOU SAYS: Truvada is a two-drug combination pill that actually does double duty in fighting HIV. As part of an HIV regimen emtricitabine and tenofovir disoproxil fumarate are combined with other HIV medicines in a drug cocktail and are potent enough to only need to be taken once a day. Bone density and kidney function will need to be monitored. Truvada is also approved for use in PrEP (see Truvada for PrEP). Mostly well tolerated, headache and nausea have been reported, but usually pass. If not, notify your healthcare provider.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$2,210.74/MONTH;
Approved as generic; not yet commercially available

Cimduo and  Temixys

3TC/TDF
lamivudine/tenofovir DF

NRTI FIXED-DOSE COMBINATION OF TWO NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NUCLEOSIDE, OR "NUKE")

★ RECOMMENDED FOR INITIAL ART FOR MOST PERSONS WHEN COMBINED WITH TIVICAY, ISENTRESS HD, OR ISENTRESS

STANDARD DOSE

One tablet once daily without regard to food for adults and children weighing at least 77 pounds (35 kg). Tablet contains 300 mg lamivudine (3TC) and 300 mg tenofovir disoproxil fumarate (TDF). Must be taken in combination with another antiretroviral(s) which does not contain the medications (or their equivalents) in this drug combination .

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

The dosing frequency needs to be adjusted for people with decreased kidney function. Cimduo and Temixys should not be used if CrCl is less than 50 mL/min or if you are on dialysis.

- SEE THE INDIVIDUAL DRUGS CONTAINED IN CIMDUO AND TEMIXYS: Epivir and Viread.
- SEE PACKAGE INSERT for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

Most common adverse events (in more than 10% of people taking it) are headache (14%), pain (13%), depression (11%), diarrhea (11%), and rash (18%) (when studied in combination with efavirenz). Rare skin discoloration on palms and soles may also occur. The TDF in Cimduo is associated with long-term decreases in bone mineral density (BMD). BMD monitoring should be considered in people who have a history of bone fracture due to disease or are at risk for osteopenia or osteoporosis. While calcium and vitamin D levels can be checked to assess the need for these supplements, talk with your provider before starting on your own. TDF can cause kidney toxicities. Tell your provider about any pain in extremities, persistent or worsening bone pain and fractures, with or without muscular pain or weakness, as well as any concerning changes in urinary habits, as these could be signs of kidney problems. Routine monitoring of estimated creatinine clearance, serum phosphorus, urine glucose, and urine protein should be performed in all individuals with mild kidney impairment. If you have HIV and HBV, guidelines recommend treatment for both viruses. Cimduo can be used to treat HIV and HBV simultaneously. If you are co-infected with HBV and HIV, you should not stop Cimduo without medical supervision because it can cause your HBV to flare and cause you to experience signs and symptoms of acute hepatitis. HBV should be closely monitored by your provider. Cimduo contains lactose, which can cause some abdominal discomfort, especially in patients sensitive to lactose.

SCAN THIS QR CODE WITH YOUR SMARTPHONE TO VIEW THIS PAGE ONLINE.

POTENTIAL DRUG INTERACTIONS

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

MORE INFORMATION

This slightly different version of Truvada was approved by the FDA in 2018. It contains 3TC instead of Truvada's FTC. The two meds are essentially equivalent. The niche for Cimduo is that it may be a cheaper option for some insurance plans because it contains generic drugs. It also allows for some new or unique co-formulations (such as with Delstrigo, Symfi, and Symfi Lo). Cimduo has received DHHS HIV treatment guidelines recommendation as a component for initial ART in most people with HIV when combined with dolutegravir or raltegravir. TDF is falling out of favor since the newer formulation tenofovir alafenamide, or TAF, was approved. TAF is safer on kidneys and bones than TDF. Unlike Truvada, Cimduo is not approved for PrEP (HIV prevention). DHHS treatment guidelines recommend Cimduo, Truvada, or Descovy (which contains TAF) over Epzicom as the preferred NRTI component for initial therapy (unless Epzicom is paired with Tivicay). Kidney function must be monitored before and during treatment with Cimduo and it may not be a good option for patients with underlying kidney problems. When the virologic efficacy of Cimduo was compared to Truvada (each combined with Sustiva or nevirapine or a boosted PI) in a study, Cimduo was associated with higher rates of virologic failure compared to Truvada when paired with an NNRTI; however, there was no difference in the rates of virologic failure when paired with a boosted PI. It should be noted the people in the study who were taking Cimduo generally had higher viral loads, lower CD4 counts, and were more likely to be using injection drugs at the start of the study compared to patients taking Truvada. Another study examining historical data noted viral resistance was more common with Cimduo than with Truvada, however this was not observed in clinical trials. Cimduo is recommended by DHHS as one of the preferred NRTI combination components of an ART regimen in pregnancy. Another drug containing the same medications as Cimduo (and at the same doses), Temixys, is FDA approved and now commercially available in the United States.

DR. ROSS SLOTTEN SAYS: Cimduo is the second generic two-nucleoside fixed-dose combination tablet approved by the FDA (generic Epzicom—lamivudine/abacavir was the first). Cimduo contains lamivudine and TDF. Combined with efavirenz, it is virtually equivalent to Atripla, although lamivudine (3TC) replaces emtricitabine (FTC). Yet what value it adds to the anti-HIV armamentarium is unclear. With TDF-containing regimens on the wane, I don't see a significant role for Cimduo in the future. Once again, lower cost is touted as its main advantage over Truvada and Descovy, but that is a misleading issue in my mind, as I mentioned earlier.

ACTIVIST BRIDGETTE PICOU SAYS: Temixys contains two medications, lamivudine and tenofovir DF. It is taken with other HIV medications and is a fixed-dose tablet, so it cannot be dose adjusted. You will also need to have your hepatitis B status monitored before starting or stopping therapy as suddenly stopping may cause your hepatitis infection to flare. Temixys can be taken with or without food. Another benefit is it should cost less than some of the other tenofovir-containing regimens. Cimduo is a lower cost alternative HIV medication. It is a fixed-dose, two-drug combo medication containing lamivudine and tenofovir DF. Some side effects like headache and depression have been reported. With the TDF component you should have regular kidney function monitoring and bone density testing. Other than that, it is considered an effective treatment when combined with other HIV medications.

MANUFACTURER

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

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

AVERAGE WHOLESALE PRICE

Cimduo: $1,206.56/MONTH
Temixys: $1,020.00/MONTH

GENERIC IS AVAILABLE.

Epzicom

ABC/3TC
abacavir/lamivudine

NRTI FIXED-DOSE COMBINATION OF TWO NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NUCLEOSIDE, OR "NUKE")

★ RECOMMENDED AS A COMPONENT OF INITIAL REGIMEN FOR MOST PEOPLE WHEN USED IN COMBINATION WITH DOLUTEGRAVIR (AS TRIUMEQ)

STANDARD DOSE

One tablet once daily, without regard to food. Tablet contains 600 mg abacavir and 300 mg lamivudine. Must be taken in combination with another antiretroviral(s) which does not contain the medications in this drug combination.

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

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

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

POTENTIAL SIDE EFFECTS AND TOXICITY

The length of this section is meant to be informative, not scary. Common side effects may include headache, nausea, fatigue, depressed mood, dizziness, diarrhea, and insomnia. Of note is the hypersensitivity reaction (HSR, an allergic-like reaction) warning on abacavir (see Ziagen for details of symptoms). To minimize the risk for HSR, a blood test for HLA-B*5701 (a genetic marker) should be done prior to starting an HIV regimen containing abacavir to identify patients at higher risk for this reaction. A negative HLA-B*5701 test does not mean you won't have HSR, but the risk is reduced to 1% or less from clinical studies. This test is covered by most insurances and also by LabCorp/ViiV (see company contact on co-pay chart).

An HSR can technically occur at any time, regardless of how long you have taken the medication, however, it is much more likely to occur when you start (or restart) the medication (90% occur within the first 6 weeks of treatment). Symptoms of an HSR usually worsen, very slowly, with every dose. Call your healthcare provider right away to find out if you should stop taking Epzicom. If you stop Epzicom because of an allergic reaction, never take Epzicom or an abacavir-containing regimen such as Triumeq or Ziagen again (called "rechallenging"). Rechallenging could cause a rare life-threatening reaction. This does not apply to a missed dose when HSR is not suspected, but talk with your healthcare provider and watch for symptoms if you've stopped the drug for at least a few days.

Some large observational studies suggest abacavir may increase the risk of cardiovascular events, including myocardial infarction (MI, or heart attack), in people with greater risk factors such as smoking, diabetes, high blood pressure, older age, high cholesterol, family history of heart disease, and drug use. Other studies have found no increased risk. To date, no absolute consensus has been reached on the association of abacavir with cardiac risk or a possible mechanism for the association. People who have high risk for heart disease should discuss risks with their provider, and they should be monitored more closely. If you have HIV and HBV, guidelines recommend treatment for both viruses. The lamivudine component of Epzicom can be used to treat HIV and HBV simultaneously. If you are co-infected with HBV and HIV, you should not stop Epzicom without medical supervision because it can cause your HBV to flare up and cause you to experience signs and symptoms of acute hepatitis. HBV should be closely monitored by your provider.

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POTENTIAL DRUG INTERACTIONS

See the individual drugs contained in Epzicom, Epivir and Ziagen. It is important to take Epzicom only with other HIV medications recommended by your provider because Epzicom and its equivalent drugs are contained in other HIV medications: Atripla, Biktarvy, Cimduo, Combivir, Complera, Delstrigo, Descovy, Emtriva, Epivir, Genvoya, Odefsey, Stribild, Symfi, Symfi Lo, Symtuza, Temixys, Triumeq, Trizivir, Truvada, or Ziagen; also Epivir-HBV used for the treatment of hepatitis B. Alcohol can increase the levels of abacavir and therefore can increase the possibility of side effects. Epzicom may be used with hepatitis C drugs Epclusa, Harvoni, or Zepatier, depending on the third drug in the HIV regimen. Avoid use of sorbitol-containing medicines with lamivudine; there are many, such as acetaminophen liquid (Tylenol liquid and others). Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions not listed here.

MORE INFORMATION

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

DR. ROSS SLOTTEN SAYS: Epzicom, which contains abacavir and lamivudine (3TC), was originally approved as a single tablet two-nucleoside backbone for HIV therapy, like Truvada. However, subsequent studies have shown that it is inferior to Truvada when given to patients with high viral loads (greater than 100,000 copies/mL). In one of its earlier iterations, Trizivir (AZT, abacavir, 3TC), 80 per cent of patients achieved and maintained undetectable viral loads as compared to other 3-drug combinations, which had a greater than 90 % success rate in maintaining maximal viral suppression. Today, most abacavir/3TC use is in combination with Tivicay (dolutegravir), which has been given an AI rating in the DHHS HIV drug guidelines because Tivicay is both potent and has a low barrier to resistance. Before prescribing Epzicom, it is critical to screen for the presence of the genetic marker HLA-B*5701, which predicts a severe allergic reaction to abacavir. Moreover, as mentioned elsewhere, there has been concern about the association of abacavir with an increased risk for heart attacks, an association that has not been definitively proven in clinically controlled studies.

ACTIVIST BRIDGETTE PICOU SAYS: Epzicom is a combination tablet containing abacavir and lamivudine (also found in Triumeq). The abacavir component has been known to cause both trouble sleeping and vivid dreams as side effects, but it is still a good alternative for those who are unable to take Truvada. There is a simple blood test that should be taken before starting Epzicom to test for an allergic sensitivity to abacavir. This is called a hypersensitivity reaction and can be fatal. Your viral load is also a consideration as with higher viral loads over 100,000 copies it may not be as effective. There are also concerns that it may increase the risk of cardiac disease.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

1,550.05/MONTH;
generic: **$1,395.05**/MONTH

Emtriva

FTC
emtricitabine

NRTI NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR (NUCLEOSIDE, OR "NUKE")

★ RECOMMENDED AS A COMPONENT OF INITIAL REGIMEN FOR MOST PEOPLE

STANDARD DOSE

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

For adults and children regardless of age; a liquid formulation is available for infants and young children. Emtriva is dosed based on body weight for children. See the package insert for weight-based dosing.

Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. It is also available as an oral solution (10 mg/mL) (cotton candy flavor) for children of any age and adults who are not able to swallow the capsules. Can be substituted for Epivir.

- **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.
- **TELL YOUR PROVIDER OR PHARMACIST** about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not.

POTENTIAL SIDE EFFECTS AND TOXICITY

Emtriva is very well tolerated. The most common side effects (rarely reported) may include headache, diarrhea, and nausea. If you have HIV and HBV, guidelines recommend treatment for both viruses. Emtriva can treat both HIV and HBV, but must be used in combination with another hep B drug (such as tenofovir) to treat the hep B. If you are co-infected with HBV and HIV, you should not stop Emtriva without medical supervision because it can cause your HBV to flare and cause you to experience signs and symptoms of acute hepatitis. HBV should be closely monitored by your provider. Rare skin discoloration (darkening of the skin on the palms and the soles) can occur and was more frequent in children, but is generally mild and not concerning.

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POTENTIAL DRUG INTERACTIONS

No significant drug interactions. Emtriva may be used with hepatitis C drugs such as Epclusa, Harvoni, or Zepatier, depending on the other components in the HIV regimen.

MORE INFORMATION

Emtriva (emtricitabine) is similar to Epivir (lamivudine): both treat HIV and HBV and have the same resistance profile, meaning that if your virus is resistant to one drug, it will be resistant to the other. If your HIV develops resistance to Epivir or Emtriva, it does not mean that your HBV is also resistant to them. Both Descovy and Truvada (both contain Emtriva) are currently recommended by DHHS HIV treatment guidelines for first-time therapy for most people. Emtriva is also found in several single-tablet regimens (Atripla, Biktarvy, Complera, Genvoya, Odefsey, Stribild, and Symtuza). Sometimes, drug resistance that the virus develops against emtricitabine makes the virus reproduce at a slower rate. This drug resistance can also improve the antiviral activity of Retrovir (zidovudine) and Viread (tenofovir), and for that reason, some providers continue Emtriva treatment in combination with other antiretrovirals after resistance develops. Emtriva oral solution should be kept in the refrigerator. If kept at room temperature, the oral solution should be used within three months. The capsule is small, which is an advantage for people with difficulty swallowing.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

200 mg, 30 capsules:
$643.82/MONTH

DR. ROSS SLOTTEN SAYS: No comment provided because of redundancy. Emtriva is almost exclusively used as part of combination tablets.

ACTIVIST BRIDGETTE PICOU SAYS: Emtriva has a good safety profile and is chemically the same as lamivudine, the difference being Emtriva (emtricitabine) has a longer half-life, which means that it is in the body longer. It can also be used as part of a treatment profile for hepatitis B although it is not a cure. Don't stop using the medication suddenly if you have hep B or don't know your hep B status. Emtriva is found in a number of STRs such as Biktarvy, Odefsey, and Symtuza and is also found in Truvada and Descovy.

GENERIC IS AVAILABLE.

Epivir

3TC
lamivudine

NRTI NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR (NUCLEOSIDE, OR "NUKE")

★ RECOMMENDED AS A COMPONENT OF INITIAL REGIMEN FOR MOST PEOPLE

STANDARD DOSE

One 300 mg tablet once daily (or one 150 mg tablet twice daily), without regard to food. Dosing needs to be adjusted for adults and children who have decreased kidney function (creatinine clearance less than 50 mL/min). This medication, however, is often used in reduced renal function below 50 due to relatively minimal risk of lamivudine accumulation and side effects. See package insert for guidance on dosing in the setting of kidney impairment. Must be taken in combination with another antiretroviral(s).

According to the package insert, it is indicated for adults and children at least 3 months of age and older. Based on pediatric DHHS guidelines, it can be used as part of an empiric HIV regimen in infants of at least 32 weeks' gestation at birth for higher risk perinatal HIV exposure. Epivir for children is dosed based on body weight. See the package insert and/or DHHS guidelines for weight-based dosing.

Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. The 150 mg tablets are scored and may be split. Based on drug properties, tablets may be crushed and added to a small amount of semi-solid food or liquid for immediate consumption. Epivir is also available as an oral solution (10mg/mL) (strawberry-banana flavor) for children and adults who are not able to swallow the tablets. Can be substituted for Emtriva.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Epivir is very well tolerated. The most common side effects were headache, diarrhea, nausea, malaise (general ill feeling), fatigue, nasal symptoms, diarrhea, and cough. If you have HIV and HBV, guidelines recommend treatment for both viruses. Epivir can treat both HIV and HBV, but must be used in combination with another hepatitis B drug (such as tenofovir) to treat the hep B. If you are co-infected with HBV and HIV, you should not stop Epivir without medical supervision because it can cause your HBV to flare up and cause you to experience signs and symptoms of acute hepatitis. HBV should be closely monitored by your provider.

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POTENTIAL DRUG INTERACTIONS

No significant drug interactions. Epivir may be used with hepatitis C drugs Epclusa, Harvoni, or Zepatier, depending on the other components in the HIV regimen. Avoid use of sorbitol-containing medicines with lamivudine; there are many, such as acetaminophen liquid (Tylenol liquid and others).

MORE INFORMATION

Epivir (lamivudine) is similar to Emtriva (emtricitabine): both treat HIV and HBV and have the same resistance profile, meaning that if your virus is resistant to one drug, it will be resistant to the other. If your HIV develops resistance to lamivudine, it doesn't mean that your HBV is also resistant to it. Sometimes, drug resistance that the virus develops against lamivudine makes the virus reproduce at a slower rate. This drug resistance can also improve the antiviral activity of Retrovir (zidovudine) and Viread (tenofovir), and for that reason, some providers continue Epivir treatment in combination with other antiretrovirals after resistance develops. Lamivudine is also available in several combination products: Cimduo and Temixys (with tenofovir DF), Combivir (with zidovudine), Epzicom (with abacavir), Trizivir (with zidovudine and abacavir), Symfi and Symfi Lo (with tenofovir DF and efavirenz), Delstrigo (with tenofovir DF and doravirine), and Triumeq (with dolutegravir and abacavir). Epivir as part of the combination tablet Combivir is recommended as an alternative NRTI combination component of an ART regimen during pregnancy. Epivir is available as generic lamivudine, which should be as effective and well tolerated as the brand name drug Epivir. Some insurers may require patients to take regimens containing generics rather than brand name drugs, including simpler co-formulated products. For example, since both zidovudine (Retrovir, AZT) and lamivudine are available in generic form, a person might have to take these two generic pills instead of the fixed-dose combination tablet Combivir. The availability of generics might also limit choices of therapy. For example, newer brand name drugs and co-formulations, such as Biktarvy, might be restricted to patients who can't physically tolerate generic regimens.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com
(877) 844-8872

AVERAGE WHOLESALE PRICE

Epivir 300 mg tablets, 30 tablets:
$498.89/MONTH
generic lamivudine 300 mg tablets, 30 tablets:
$429.66/MONTH

DR. ROSS SLOTTEN SAYS: No comment provided because of redundancy. Epivir is almost exclusively used as part of combination tablets.

ACTIVIST BRIDGETTE PICOU SAYS: Still in use today, Epivir is an effective part of an HIV regimen, with the added benefit of being able to be used as part of treatment therapy if you're co-infected with hepatitis B. Even though it is one of the oldest HIV medications still being used, it is well tolerated with few side effects. There are no drug-drug interactions associated with it. A notable downside is that an HIV mutation—M184V—can reduce how well it works. Lamivudine is also a component of Triumeq and Dovato.

GENERIC IS AVAILABLE.

Viread

TDF
tenofovir disoproxil fumarate

NRTI NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR (NUCLEOSIDE, OR "NUKE")

★ RECOMMENDED AS A COMPONENT OF INITIAL REGIMEN FOR MOST PEOPLE

STANDARD DOSE

One 300 mg tablet once daily, without regard to food in adults and children at least 2 years old weighing at least 21 pounds (10 kg). Viread tablets are also available in the following dosages: 150 mg, 200 mg, 250 mg tablets, and oral powder (40 mg/g in 60 g packets). Viread tablets can be disintegrated in water, grape juice, or orange juice with minor stirring and pressure from a spoon. In children, Viread is dosed based on body weight. See package insert for specific weight-based dosing. Must be taken in combination with another antiretroviral(s).

Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. Dosing frequency needs to be adjusted for adults and children with decreased kidney function (for creatinine clearance, or CrCl, less than 50 mL/min). See package insert for guidance on dosing in the setting of kidney impairment. FDA approved for chronic HBV in patients 12 years and older weighing at least 77 pounds (35 kg).

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Generally well tolerated, but some may experience nausea, diarrhea, vomiting, and gas. Decreases in bone mineral density (BMD) have been observed. BMD monitoring should be considered in people who have a history of bone fracture due to bone disease or are at risk for osteopenia or osteoporosis. Viread may cause kidney toxicities. Creatinine clearance (CrCl) should be assessed before initiating treatment. In addition to CrCl, glucose and protein in the urine and serum phosphorus should be monitored more often in patients at risk for kidney problems. Tell your provider about any pain in extremities, persistent or worsening bone pain and fractures, with or without muscular pain or weakness, as well as any concerning changes in urinary habits, as these could be signs of kidney problems. If you have HIV and HBV, guidelines recommend treatment for both viruses. Viread can treat both HIV and HBV, but must be used in combination with another hep B drug (such as Emtriva) to treat the hep B. If you are co-infected with HBV and HIV, you should not stop Viread without medical supervision because it can cause your HBV to flare and cause you to experience signs and symptoms of acute hepatitis. HBV should be closely monitored by your provider. The Viread formulation contains lactose, which can cause some abdominal discomfort, especially in patients sensitive to lactose.

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POTENTIAL DRUG INTERACTIONS

Viread decreases the levels of Reyataz; therefore, Reyataz 300 mg must be boosted with Norvir 100 mg or Tybost 150 mg (taken together with food) when used in combination with TDF. Kaletra, Prezista/Norvir, and Reyataz/Norvir increase Viread levels, but there is no dose adjustment needed. Patients taking Kaletra, Prezista/Norvir, or Reyataz/Norvir with TDF should be monitored for Viread side effects (including kidney disorders) due to the higher TDF levels. Do not take Viread with adefovir. Avoid taking Viread with drugs that negatively affect the kidneys, including chronic use or high doses of NSAIDS (nonsteroidal anti-inflammatory drugs for pain, such as Advil or Motrin (ibuprofen) and Aleve (naproxen). Viread may be used with hepatitis C drugs such as Harvoni or Zepatier, depending on the other components in the HIV regimen. Monitor for tenofovir toxicities if used with Epclusa. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not.

MORE INFORMATION

TDF with emtricitabine (as Truvada) and TDF with lamivudine (as Cimduo or Temixys) are recommended NRTI combinations by DHHS HIV treatment guidelines for first-time therapy. A new version of tenofovir, called tenofovir alafenamide (TAF), replaced TDF in certain fixed-dose combinations. Biktarvy, Genvoya, Odefsey, and Symtuza are four single-tablet regimens containing TAF instead of TDF. Descovy is another version of Truvada, combining emtricitabine with TAF instead of TDF. In clinical trials, TAF had fewer kidney and bone issues than TDF. The NIH reported infants exposed in the womb to TDF may have lower bone mineral content than those exposed to other antivirals. Tenofovir DF was approved in 2012 as part of Truvada for HIV prevention as PrEP (pre-exposure prophylaxis; see Truvada for PrEP page). TDF is part of the single-tablet regimens Atripla, Symfi, Symfi Lo, Complera, Delstrigo, and Stribild as well as the fixed-dose combination tablets Cimduo and Temixys. Viread is part of the combination tablets Truvada, Cimduo, and Temixys, which are recommended by DHHS as part of the preferred NRTI combination components of an ART regimen in pregnancy.

DR. ROSS SLOTTEN SAYS: No comment provided because of redundancy. Viread is almost exclusively used as part of combination tablets.

ACTIVIST BRIDGETTE PICOU SAYS: Viread, more commonly known as tenofovir disoproxil fumarate (TDF), is a component of Truvada. It is also found in several STRs. TDF has been known to cause kidney toxicity and bone density loss, so monitoring will need to be done while taking the medication. Often the symptoms of the kidney problems will disappear once the medication is discontinued. The newer formulation of the drug is called TAF, and has a better safety profile and is becoming more widely used. Even with this, TDF is mostly well tolerated. Side effects should be minimal.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

300 mg tablets:
$1,504.20/MONTH
generic 300 mg tablets:
$1,151.82/MONTH

GENERIC IS AVAILABLE.

Ziagen ABC abacavir

NRTI NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR (NUCLEOSIDE, OR "NUKE")

★ RECOMMENDED AS A COMPONENT OF INITIAL REGIMEN FOR MOST PEOPLE WHEN USED IN COMBINATION WITH DOLUTEGRAVIR AND LAMIVUDINE (AS TRIUMEQ)

STANDARD DOSE

Two 300 mg tablets once daily (or one 300 mg tablet twice daily), without regard to food. For adults and children at least 3 months of age and older. In children Ziagen is dosed based on body weight. See the package insert for weight-based dosing. Tablets may be crushed or split and added to a small amount of semi-solid food or liquid. Ziagen is also available as an oral solution (20 mg/mL) (strawberry-banana flavor) for children and adults who are not able to swallow the tablets. Must be taken in combination with another antiretroviral(s).

Dose adjustment is not needed for people with kidney impairment. Dose adjustment is needed for people with mild liver impairment (200 mg twice daily). Ziagen should not be used in people with moderate or severe liver disease.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

The length of this section is meant to be informative, not scary. The most common side effects with an incidence greater than 10% were nausea, headache, malaise (general ill feeling), fatigue, vomiting, and dreams/sleep disorders. In pediatric patients, the more common side effects were fever and/or chills, nausea and vomiting, skin rashes, and ear/nose/throat infections.

Approximately 8% of people who took abacavir in clinical trials (where screening for HLA-B*5701, a genetic marker associated with abacavir hypersensitivity, was not performed) experienced hypersensitivity reaction (HSR), an allergic-like reaction. To minimize the risk for HSR, a blood test for HLA-B*5701 should be done prior to starting an HIV regimen containing abacavir to identify patients at higher risk for this reaction. This test is covered by most insurance and also by LabCorp/ViiV (GO TO viivconnect.com). If the HLA-B*5701 test is positive, you are at an increased risk for HSR and you should not take abacavir. An allergy to it should be entered in your medical record. A negative HLA-B*5701 test does not mean you won't have HSR, but the risk is very low (1% from clinical studies). Symptoms of HSR usually include some combination of the following: fever, skin rash, malaise (general ill feeling), severe nausea, headache, muscle ache, chills, diarrhea, vomiting, abdominal pain, respiratory symptoms (cough, difficulty breathing, sore throat), and/or joint pain. Symptoms are listed on the patient information sheet and warning card that you receive each time you fill your prescription. You should keep the warning card with you. HSR might be confused with flu, but symptoms of HSR usually worsen, very slowly, and with every dose.

People who think they are experiencing HSR must be evaluated by an experienced HIV provider right away before they stop taking abacavir. Do not use a skin patch test to confirm HSR. Symptoms usually resolve after permanent discontinuation. If you develop HSR, abacavir should be stopped and you can never take abacavir or any product containing abacavir (Epzicom, Ziagen, or Triumeq) again (starting again is called rechallenging). Rechallenging can cause a rare life-threatening reaction. This does not apply to a missed dose when there is no HSR, but talk with your healthcare provider and watch for symptoms if you've stopped the drug for a few days, preferably under the observation of others who can call for medical help if you develop symptoms. An HSR can technically occur at any time, regardless of how long you have been taking the medication, however, it is much more likely to occur when you start (or re-start) the medication (90% occur within the first 6 weeks of treatment).

Some large observational studies suggest abacavir may increase the risk of cardiovascular events, including myocardial infarction (MI, or heart attack), in people with risk factors (such as older age, smoking, diabetes, high blood pressure, high cholesterol, family history of heart disease, and drug use), especially within the first 6 months of therapy. However, other studies, including a large meta-analysis, have shown no increase in cardiovascular risk. To date, no absolute consensus has been reached on the association of abacavir with cardiac risk or a possible mechanism for the association. People who are at high risk for heart disease should discuss risks with their provider and they should be monitored more closely.

DR. ROSS SLOTTEN SAYS: No comment provided because of redundancy. Ziagen is almost exclusively used as part of combination tablets.

ACTIVIST BRIDGETTE PICOU SAYS: Abacavir is taken in conjunction with other HIV meds and should not be taken alone. There is a simple blood test that should be taken before starting Ziagen to test for an allergic sensitivity. This is called a hypersensitivity reaction and can be fatal. There are potentially serious side effects associated with the medication for some people, so monitor how you feel while taking it. If you feel like you are developing or have symptoms of an allergic reaction, stop taking the medication and notify your provider. Liver problems and lactic acidosis, which is a buildup of acid in the blood, can happen. Liver function should be monitored while taking Ziagen.

POTENTIAL DRUG INTERACTIONS

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

MORE INFORMATION

The ACTG A5202 study found that abacavir/lamivudine (Epzicom) was inferior to tenofovir/emtricitabine (Truvada) in getting people undetectable when their pre-treatment viral load was over 100,000 copies/mL. However, when combined with Tivicay (dolutegravir), Epzicom performed just as well as Truvada in people with high viral loads (over 100,000 copies/mL). Hence, Triumeq is the only abacavir-containing regimen recommended by DHHS as initial therapy for most HLA-B*5701 negative people. It is recommended people with symptoms of acute respiratory disease consider HSR even if another diagnosis such as pneumonia, bronchitis, or flu is possible. But again, a simple test reveals whether you are at high risk for the allergic reaction. FDA researchers reported finding a mechanism for autoimmune drug reactions, including abacavir HSR, and hope it helps improve drug safety in the future. Ziagen as part of the combination tablet Epzicom is recommended by DHHS as one of the preferred NRTI combination components of an ART regimen during pregnancy.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com
(877) 844-8872

AVERAGE WHOLESALE PRICE

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

SCAN THIS QR CODE WITH YOUR SMARTPHONE TO VIEW THIS PAGE ONLINE.

Edurant

RPV
rilpivirine

NNRTI NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR (NON-NUCLEOSIDE, OR "NON-NUKE")

✔ RECOMMENDED AS A COMPONENT OF INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS IN COMBINATION WITH DESCOVY OR TRUVADA (AS ODEFSEY OR COMPLERA)

STANDARD DOSE

One 25 mg tablet once daily with a meal. For adults and children (12 years of age and older weighing at least 77 pounds, or 35 kg) taking HIV treatment for the first time (treatment-naïve). Must be taken in combination with another antiretroviral(s) which does not contain this medication or medication from the same drug class. No dose adjustment needed for pregnant patients with undetectable viral load on a stable rilpivirine-based regimen, but monitor viral load closely because lower rilpivirine drug exposure has been observed during pregnancy.

Viral load (HIV RNA) must be less than 100,000 copies/mL and CD4 T cell count must be above 200 cells/mm^3 before starting Edurant due to higher rates of virologic failure in these patients.

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

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

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

POTENTIAL SIDE EFFECTS AND TOXICITY

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

POTENTIAL DRUG INTERACTIONS

Edurant cannot be taken with the anti-seizure medications carbamazepine, oxcarbazepine, phenobarbital, or phenytoin; the anti-TB drugs rifampin and rifapentine; proton pump inhibitors (Aciphex, Dexilant, Nexium, Prevacid, Protonix, and Prilosec); or the herb St. John's wort. Do not take with more than one oral dose of the steroid dexamethasone. 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 like fluconazole, itraconazole, ketoconazole, posaconazole, and voriconazole; dose adjustment for these medications may be needed. Use azithromycin when possible instead of the antibiotics clarithromycin, erythromycin, and telithromycin. Methadone levels are reduced slightly and patients should be monitored for symptoms of withdrawal. Edurant should be used with caution when taken with other medications with a known risk of torsades de pointes or QT prolongation (these abnormal heart rhythms can make the heart stop). No dose adjustment needed with hepatitis C medications Epclusa, Harvoni, or Zepatier.

DR. ROSS SLOTTEN SAYS: No comment provided because of redundancy. Edurant is almost exclusively used as part of combination tablets.

ACTIVIST BRIDGETTE PICOU SAYS: Rilpivirine can be found in several of the single-tablet regimens used today, and also in the soon-to-be-approved once- or twice-monthly injectable with cabotegravir called Cabenuva. In pill form it needs to be taken with a meal. It is well tolerated and often best used as a switch regimen for stable persons with an undetectable viral load. There are drug-drug interactions so communicate what you are taking to your doctor, especially antacids, whether prescribed or over-the-counter. Take as directed daily to avoid resistance, which can cause cross resistance with another HIV medication (etravirine).

MORE INFORMATION

A newer medication combining rilpivirine with dolutegravir was approved by the FDA in late 2017; see Juluca. A long-acting injectable formulation of rilpivirine may be approved this year along with a long-acting injectable formulation of cabotegravir to form a complete regimen given once a month; see the long-acting cabotegravir/long-acting rilpivirine page. Edurant is not recommended for treatment-naïve patients with a pre-treatment viral load greater than 100,000 copies/mL or CD4 less than 200 cells/mm^3. A rilpivirine-based regimen may be advantageous in people with high risk for heart disease due to its relatively low impact on lipid profile. The clinical benefits, however, are not known at this time. While its tolerability and safety profiles are advantages for Edurant, the greater potential for virologic failure in patients with high viral loads or low CD4 counts, 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 in 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.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$1,398.35/MONTH

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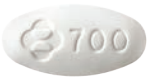

Pifeltro DOR doravirine

NNRTI NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR (NON-NUCLEOSIDE, OR "NON-NUKE")

✔ RECOMMENDED AS A COMPONENT OF INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS (AS A COMPONENT OF DELSTRIGO, OR IN COMBINATION WITH DESCOVY, TRUVADA, CIMDUO, OR TEMIXYS)

STANDARD DOSE

One 100 mg tablet once daily without regard to food in combination with other antiretroviral drugs in people taking HIV treatment for the first time (treatment-naïve) or to replace the current antiretroviral regimen in those who are virologically suppressed (HIV viral load less than 50 copies/mL) on a stable antiretroviral regimen with no history of treatment failure and no known viral substitutions associated with resistance to doravirine. Must be taken in combination with another antiretroviral(s) which does not contain this medication or medication from the same drug class.

Approved only for adults at this time. Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. No dosage adjustment necessary for mild, moderate, or severe kidney impairment or for mild or moderate liver impairment. Pifeltro has not been studied in patients with severe liver impairment.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Most common side effects observed with Pifeltro in studies were nausea (7%), dizziness (7%), headache (6%), fatigue (6%), diarrhea (5%), abdominal pain (5%), and abnormal dreams (1%). Rash, which is a common side effect of the NNRTIs, was reported in up to 2% of the studied population. In one study (DRIVE-AHEAD), an in-depth analysis was conducted of the incidence of neuropsychiatric adverse events associated with a doravirine-containing regimen (Delstrigo) compared to Atripla. Neuropsychiatric events, such as depression, sleep disturbances, and dizziness, are another common side effect of the NNRTI class. Doravirine did not appear to negatively affect cholesterol in studied populations.

POTENTIAL DRUG INTERACTIONS

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

MORE INFORMATION

Received FDA approval in 2018. Doravirine may be an option for patients who have developed drug resistance to other NNRTIs. A single-tablet regimen (STR) containing doravirine was also approved in 2018; see Delstrigo page. Delstrigo, however, contains the older version of tenofovir, tenofovir DF. The stand-alone Pifeltro allows people to take it with the newer tenofovir alafenamide, or TAF (found in Descovy), which has potentially less renal and bone toxicity. On the other hand, of course, the use of Pifeltro means the necessity for an extra pill, such as Descovy, or maybe more than one extra pill, depending on the regimen being used. Pifeltro was found to be non-inferior to boosted darunavir (Prezista) as well as efavirenz (Sustiva) at 48 weeks. Doravirine was superior to boosted darunavir at week 96 in terms of virologic suppression, but it should be noted there was a higher rate of study discontinuation in the boosted darunavir group. Doravirine is a non-nucleoside medication, and it should be noted that this class of drugs typically has a lower barrier to resistance as well as has 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 with both boosted darunavir and efavirenz. It also has fewer potential drug interactions than efavirenz or rilpivirine, and, unlike rilpivirine, virologic efficacy is not compromised in those with high baseline viral loads or low CD4 counts. Doravirine has not been directly compared to integrase inhibitor-based regimens in clinical trials yet. Pifeltro now has a switch indication, so that people with undetectable viral load on a stable HIV treatment can switch to a regimen that includes Pifeltro if they have no drug resistance to it and no history of treatment failure.

DR. ROSS SLOTTEN SAYS: Pifeltro (doravirine) was approved by the FDA in August 2018 as another second generation NNRTI, like rilpivirine and etravirine (Intelence). It is taken once daily, has few side effects, and may be effective if a person is resistant to the first generation NNRTIs, efavirenz and nevirapine. However, like efavirenz and nevirapine, it has a relatively low barrier to resistance and resistance to it has already been reported. One virtue is that it can be taken with food or on an empty stomach, like bictegravir, dolutegravir, and raltegravir. It is primarily being promoted as part of the three-drug regimen, Delstrigo.

ACTIVIST BRIDGETTE PICOU SAYS: Pifeltro (doravirine) has no restrictions on CD4 count or viral load and is indicated for individuals starting therapy for the first time, and also as a switch regimen for persons stable and surpressed on current therapy. It should be taken with other ART medications and seems to be well tolerated. Additionally, it does not have the restrictions for use with proton pump inhibitors (antacids). Pifeltro is part of the single-tablet regimen Delstrigo. It seems to be well tolerated.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$1,738.80/MONTH

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GENERIC IS AVAILABLE.

Sustiva EFV efavirenz

NNRTI NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR (NON-NUCLEOSIDE, OR "NON-NUKE")

✔ RECOMMENDED AS A COMPONENT OF INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS (AS A COMPONENT OF ATRIPLA, SYMFI, OR SYMFI LO, OR IN COMBINATION WITH DESCOVY, TRUVADA, CIMDUO, OR TEMIXYS)

STANDARD DOSE

One 600 mg tablet once daily, preferably on an empty stomach at bedtime. Must be taken in combination with another antiretroviral(s) which does not contain this medication or medication from the same drug class.

Approved for adults and children 3 months and older weighing at least 7.7 pounds (3.5 kg). For children weighing less than 88 pounds (40 kg), the dose is based on weight. See the package insert for specific weight-based dosing. For children weighing at least 88 pounds, use the standard adult dose. For those who can't swallow capsules, administer by capsule sprinkle method. See below or drug label for instructions or watch the video at sustiva.com.

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

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

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

POTENTIAL SIDE EFFECTS AND TOXICITY

Central nervous system (CNS) side effects (dizziness, insomnia, impaired concentration, abnormal or vivid dreams, and hallucinations) are most common at the start of treatment and usually diminish in two to four weeks. Bedtime dosing on an empty stomach can help reduce symptoms. Less common psychiatric symptoms (catatonia, depression, suicidal thoughts or actions, aggression, paranoid/manic reactions) may also occur. A 2014 study reviewed four previously published AIDS Clinical Trials Group (ACTG) studies regarding efavirenz and suicidal ideation and re-emphasized efavirenz has an association with suicidality (reported suicidal ideation or attempted or completed suicide), and should be used with caution in patients with severe or uncontrolled depression and/or a history of suicidality. It is recommended for anyone on a regimen containing efavirenz to be regularly screened for depression and suicidality. Additional side effects may include rash, nausea, vomiting, diarrhea, and fever. Rash in 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 has not been supported in meta-analyses. The pregnancy recommendation is that women in their first trimester continue taking efavirenz as long as their viral load remains undetectable; however, efavirenz should only be used if the potential benefit outweighs the potential risk, as when other treatment options are not available. Because of the association with suicidality and neuropsychiatric effects, it is also recommended to screen for antenatal and postpartum depression in women with HIV who are taking a regimen containing efavirenz. Regular monitoring for increased liver enzyme levels is recommended initially and during treatment for people with hepatitis B/C or liver disease.

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POTENTIAL DRUG INTERACTIONS

Do not take with midazolam, pimozide, ergot derivatives, St. John's wort, or triazolam. May affect warfarin levels. Can decrease levels of buprenorphine and methadone—monitor for withdrawal. Increase Kaletra to two 200/50 mg tablets plus one 100/25 mg tablet twice daily (total 500/125 mg twice daily) with food when taken with Sustiva. Kaletra cannot be taken once daily with Sustiva. When using with Tivicay, increase the Tivicay dose to 50 mg twice daily. Treatment-experienced people should not take Reyataz with Sustiva, but for treatment-naïve people, Reyataz once-daily dose should be 400 mg with Norvir boost. Boost once-daily Lexiva 1,400 mg with 300 mg Norvir. No change in the ritonavir dose is required when efavirenz is administered with Lexiva plus ritonavir twice daily. 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. When taken with carbamazepine, phenobarbital, or phenytoin, periodic monitoring of anticonvulsant and Sustiva levels should be done or alternative anti-seizure drugs, such as levetiracetam, should be considered. Effectiveness of birth control pills may be decreased; consider the use of other contraceptives. Closer monitoring and dose adjustments may be required with posaconazole (avoid unless benefit outweighs potential risk) and itraconazole. The dose of voriconazole should be increased to 400 mg every 12 hours and the Sustiva dose should be decreased to 300 mg once daily using capsules; tablets should not be broken. Monitor effectiveness of clarithromycin or consider using azithromycin instead. Levels of immunosuppressants should be monitored when starting or stopping Sustiva. Cardizem, Lipitor, Pravachol, and Zocor doses may need to be adjusted. Titrate dose of bupropion and sertraline based on clinical response. Should not be taken with other medications that prolong QT interval or medications with a known risk of torsades de pointes. No dose adjustment with Harvoni. Don't take with Epclusa or Zepatier. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

DR. ROSS SLOTTEN SAYS: A word to the wise: Woe to any drug that claims to be king today because an upstart will one day replace you. AZT, Crixivan, and Kaletra—who praises you now? Yes, you saved people's lives—no small achievement—but at a price. Sustiva will soon join their ranks, though it remains the most commonly prescribed antiretroviral agent in the world. It's a great drug—highly potent and taken once daily. Through the marketing genius of Gilead, we HIV health care providers started prescribing it in combination with TDF and FTC well before those three medications were combined into the first single-tablet regimen, Atripla, because we knew where Gilead was heading. For almost a decade, Atripla led the pack. Sustiva's great stumbling block is the weird neuropsychiatric side effects it induces in some people living with HIV—vivid dreams, depression, even increased suicidal thoughts. Efavirenz is safe in pregnancy and doesn't interact with medications used to treat tuberculosis. Its ultimate fate will be as a niche drug, used only in special circumstances.

ACTIVIST BRIDGETTE PICOU SAYS: Sustiva is in the non-nucleoside reverse transcriptase inhibitor or NNRTI category. It is part of the combination pill Atripla or may be taken as a single tablet component with other HIV medications. Side effects may include headache, depression, feeling tired and trouble sleeping but these may ease after taking it for a few weeks. Others report the side effects just become tolerable. Remember that it's important to discuss and report all side effects with your provider. It's always good to have these conversations as the goal of therapy is tolerability with the fewest side effects possible so that you can stay adherent to your regimen.

MORE INFORMATION

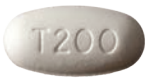
If you can't sleep, ask your doctor about gradually adjusting the timing of your dose until it's taken during the day. A rare genetic trait affecting drug metabolism of Sustiva, leading to a higher rate of side effects, occurs more in African Americans. In pediatric HIV guidelines, Sustiva was downgraded in 2017 from "preferred" to an "alternative" component of an initial regimen for children ages 3–12 years. For individuals with HIV-2, commonly found in some other countries, an NNRTI would not be recommended as HIV-2 is inherently resistant to NNRTIs. Efavirenz is found in the single-tablet regimens Atripla, Symfi, and Symfi Lo; see those pages.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

600 mg tablets:
$1,176.74/MONTH
generic: **$1,117.90**/MONTH



Intelence ETR etravirine

NNRTI NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR (NON-NUCLEOSIDE, OR "NON-NUKE")

✔ FOR TREATMENT-EXPERIENCED PATIENTS WITH VIRAL STRAINS RESISTANT TO AN NNRTI AND OTHER ANTIRETROVIRAL DRUGS ONLY

STANDARD DOSE

One 200 mg tablet, twice daily following a meal. Approved for adults and children 2 years and older weighing at least 22 pounds (10 kg). See the package insert for specific weight-based dosing in children. Also available in 25 mg and 100 mg tablets. Must be taken in combination with another antiretroviral(s) which does not contain medication from the same drug class.

Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. People unable to swallow pills (Intelence tablets are "chalky") can dissolve tablets in 1 teaspoon (5 mL) of water or at least enough liquid to cover the medication, stir well until the water turns milky, add more water if desired—use orange juice or milk as an alternative, always placing tablets in water first. Avoid warm (over 104° F) or carbonated beverages. Drink immediately, rinse the glass several times with water, orange juice, or milk and completely swallow the rinse each time to make sure the entire dose is taken. Taking Intelence without food could result in a 50% decrease in the drug absorption and may lead to HIV drug resistance.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

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

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POTENTIAL DRUG INTERACTIONS

If Intelence is taken in combination with a protease inhibitor, the PI must be boosted with low-dose Norvir. Avoid Intelence with boosted Aptivus or Lexiva. It 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. Dosage 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 those who are also taking a boosted PI. 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.

MORE INFORMATION

For patients who have had virologic failure on an NNRTI-containing regimen, do not use Intelence in combination with a nucleoside backbone alone. Although taking once daily is not FDA approved, some providers are prescribing Intelence once daily (2 of the 200 mg tablets) based on clinical trials that showed that once-daily Intelence was not inferior to Sustiva-based regimens. In Europe, it is approved as a once-daily medication; in fact, it has a half-life of 41 hours—that's a long time for the drug to completely leave the body. The once-daily dosing may improve patient adherence. The TRIO study reported the combination of Intelence with Prezista/Norvir and Isentress in highly treatment-experienced patients was successful in getting many patients to undetectable. Some patients complain of hard-to-swallow, large chalky pills; see dissolving instructions in dose section or package insert. For individuals with HIV-2, commonly found in some other countries, an NNRTI would not be recommended as HIV-2 is inherently resistant to NNRTIs. DHHS guidelines do not recommend the use of etravirine in treatment-naïve pregnant females. Females who become pregnant while taking etravirine may continue if viral suppression is effective and the regimen is well tolerated. The pharmacokinetics of etravirine are not significantly altered during pregnancy and no dosage adjustment is necessary. Etravirine is known to have a variable (moderate to high) level of transfer across the human placenta, although insufficient data exists to evaluate the effects on a fetus. Providers are encouraged to enroll pregnant females exposed to antiretroviral medications as early in pregnancy as possible in the Antiretroviral Pregnancy Registry (800-258-4263; apregistry.com).

DR. ROSS SLOTTEN SAYS: Intelence (etravirine) is another niche drug, a second generation NNRTI like rilpivirine and doravirine. It must be prescribed twice daily, so its only role is in the treatment of people with multi-drug resistant HIV, especially in those patients who can no longer take an NRTI. Intelence can be combined effectively with Prezista and/or an INSTI. Thank goodness for drugs like Intelence, even if we're not likely to prescribe them. They offer life-saving alternatives for patients who can't take AI or BI therapies.

ACTIVIST BRIDGETTE PICOU SAYS: Intelence (etravirine) is used as part of an HIV cocktail although its drug-drug interactions can make it complicated. This makes it especially important to discuss with your provider what medications you take including over-the-counter medications and any supplements. As a second generation NNRTI, it is an alternative treatment for treatment-experienced individuals and should not be taken by those who are treatment-naïve. Etravirine may be dissolved in water if the large pill size makes it difficult to swallow.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

200 mg tablets, 60 tablets:
$1,660.58/MONTH

Selzentry

MVC
maraviroc

EI ENTRY/ATTACHMENT INHIBITOR: ENTRY INHIBITOR: CCR5 ANTAGONIST

▼ NOT RECOMMENDED AS A COMPONENT OF AN INITIAL REGIMEN

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). Approved for adults and children at least two years old weighing at least 22 pounds (10 kg) and having a creatinine clearance of at least 30mL/min (measurement of kidney function); dose depends on weight. Available in a 20 mg/mL oral solution as well as 25 mg and 75 mg tablets. The oral solution should be administered using the included press-in bottle adapter and oral dosing syringe. Can be taken without regard to food. Must be taken in combination with another antiretroviral(s).

Take missed dose as soon as possible, unless it is closer in time to your next dose. Do not double up on your next dose. Before you start Selzentry, you will need a specific blood test called a Trofile to determine if this medication will work for you.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

The most common side effects occurring in greater than 8% of studied patients include cough, pyrexia (fever), upper respiratory tract infections, rash, musculoskeletal symptoms, abdominal pain, and dizziness. Other less common side effects may include allergic reactions, liver toxicity, and heart problems in those with a history of heart disease. Rarely, Selzentry can cause dizziness or fainting when standing up due to low blood pressure. Caution should be used when administering Selzentry in people with a history of or risk factors for postural hypotension, cardiovascular co-morbidities, or on 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 levels 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 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).

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POTENTIAL DRUG INTERACTIONS

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

MORE INFORMATION

Not recommended by DHHS as a component of an initial regimen due to requirement of CCR5 tropism 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 other 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 patients 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. Selzentry appears to be synergistic with Trogarzo for people with extensive HIV drug resistance. See ibalizumab page. A tropism assay (Trofile, Trofile DNA, or HIV-1 Coreceptor Tropism with Reflex to UDS) is needed to determine if this medication will work for you. Results of a phenotypic tropism test (Trofile or Trofile DNA) may take up to a month to complete. Genotypic tests are also available and may provide a faster and less expensive alternative. Selzentry only works for those people with CCR5-tropic virus. Viral tropism refers to the types of HIV that a person can have, CCR5 (R5), CXCR4 (X4), or Dual-Mix Tropic (R5 and X4). Selzentry blocks CCR5, a receptor on the outside of a CD4 cell, and shuts down this point of entry for the virus. Most people are infected with R5 virus initially, and then over time, X4 and mixed viruses may predominate. Blocking R5 with Selzentry does not cause a shift to X4 or negatively affect disease progression or CD4 count in people whose virus can use dual-mix. The tropism test needed is now generally paid for by public health departments, Medicare, and private insurances. 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 in treatment-naïve pregnant women. Women who become 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 exists to evaluate the effects on a fetus. Providers are encouraged to enroll pregnant women exposed to antiretroviral medications as early in pregnancy as possible in the Antiretroviral Pregnancy Registry (800-258-4263; apregistry.com).

DR. ROSS SLOTTEN SAYS: Why include this medication in the Drug Guide? It is not a first-line agent because not everyone can take it. Only those with a so-called CCR5 tropic virus will benefit from it; those with a CXCR4 or dual-tropic virus will not respond to it. That makes testing for susceptibility complicated and expensive. It also interacts with boosted PIs and INSTIs and other medications, so its dose has to be adjusted, which is a pain in the neck. It belongs to the entry inhibitor class of HIV medications, related to Fuzeon (enfuvirtide), which rose quickly to fame after its approval in 2003 before fizzling out because it has to be injected twice daily and causes unpleasant injection site reactions. Otherwise, Fuzeon has very few side effects, its high tolerability being a significant virtue. At the time, Fuzeon offered a life-saving alternative agent for people with HIV who had failed a good number of previous regimens. Too bad it can't be given orally. Selzentry, far fussier than Fuzeon, will remain a niche drug, useful primarily for those who have failed multiple anti-HIV regimens.

ACTIVIST BRIDGETTE PICOU SAYS: Selzentry (maraviroc) is in the entry inhibitor class of HIV medications and because of its mechanism of action is beneficial for the treatment-experienced because of how HIV adapts in the body. Selzentry works as a CCR5 antagonist to help block the virus from entering the cell. Once a person has been on medication therapy the virus may adapt to target a different entry point—CXCR4—which means Selzentry loses its advantage. There is a blood test that helps determine CCR5 activity. Dose adjustments are needed with some medications, including some HIV meds, so discuss all prescribed medications and remember to let your provider know if these changes or others are added after starting Selzentry.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

300 mg tablets, 60 tablets:
$1,874.44/MONTH

Trogarzo

IBA
ibalizumab-uiyk

EI LONG-ACTING ENTRY INHIBITOR: CD4 POST-ATTACHMENT INHIBITOR

▼ FOR HEAVILY TREATMENT-EXPERIENCED PEOPLE

STANDARD DOSE

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

The first infusion takes at least 30 minutes. If no infusion-related adverse events occur, subsequent infusions take 15 minutes. Doses may be administered every two weeks at an inpatient and/or outpatient setting, including at-home infusion, if desired. All patients should be observed for 1 hour after completing first infusion. If no infusion-associated adverse reaction is noted, the post-infusion observation time can be reduced to 15 minutes. Must be given with an optimized background regimen (OBR). An OBR consists of the best antiretroviral therapy that can be made for each patient based on the patterns of HIV drug resistance of their virus. Dose modifications of Trogarzo are not required when administered with any other antiretroviral or any other treatments.

If a maintenance dose of Trogarzo is missed by 3 days or longer beyond the scheduled dosing day, a loading dose (2,000 mg) should be administered as early as possible. Then resume maintenance dosing (800 mg) every 14 days thereafter.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

The most common adverse reactions observed in clinical studies were diarrhea (8%), dizziness (8%), nausea (5%), and rash (5%). Additionally, select lab abnormalities noted to occur in at least 5% of studied patients were increased bilirubin (greater than 2.6 times ULN—upper limit of normal) (5%), increased creatinine (greater than1.8 times ULN or 1.5x baseline) (10%), increased lipase (greater than 3 times ULN) (5%), decreased leucocytes (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 ibalizumab. Renal impairment is not anticipated to impact the pharmacokinetics of ibalizumab.

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POTENTIAL DRUG INTERACTIONS

Based on Trogarzo's mechanism of action and pharmacokinetic profile, drug-drug interactions are not expected. No 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). 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. U.S. HIV treatment guidelines list Trogarzo this way: "Patients with ongoing detectable viremia [detectable viral load] who lack sufficient treatment options to construct a fully suppressive regimen [get to undetectable viral load] may be candidates for the recently approved CD4 post-attachment inhibitor ibalizumab."

Ibalizumab is a shiny new option, but it doesn't come without some rules. It is expensive because the cost of the drug will be added to other expenses such as the time at the infusion center and qualified individuals to administer and handle the medication, although there may be an option for patients to receive their infusion at home. Non-adherence won't be an option—people won't be able to just show up whenever they want or be late to appointments when going to an infusion center. Patients must be on time.

Although given once every two weeks, because it must be used with other HIV medications, antiviral treatment will still be required to be taken daily. Ibalizumab is also the first HIV orphan drug—one that is produced for a relatively small population of patients (fewer than 200,000). It was produced for people with multi-drug resistant HIV, estimated to be fewer than 40,000 in the U.S.; the company estimates that there are fewer than 25,000. These are heavily treatment-experienced people who have multi-drug resistance, and have therefore, limited treatment options. Ibalizumab has been shown to work against highly drug-resistant virus, when combined with an OBR. A poster presentation at CROI 2019 showed long-term (96 week) data whereby the safety and efficacy observed at 24 weeks were maintained at Week 96. Fifteen of the 27 participants who continued in the long-term study had achieved undetectable viral load (less than 50 copies) at Week 24, and 16 were undetectable at Week 96. Furthermore, twelve patients who rolled over from a previous Phase 2 study have been on treatment with ibalizumab for an average of 8.8 years (7.8–9.5 years). For the study, as part of the OBR, investigational antivirals, including fostemsavir (see fostemsavir page), were allowed.

DR. ROSS SLOTTEN SAYS: We should be thankful that a drug like Trogarzo exists. It has a novel mode of action—a monoclonal antibody, it prevents HIV from entering the CD4+ (T helper) cells, regardless of tropism (whether CCR5, CXCR4, or dual tropic). It is given as an intravenous infusion every two weeks. Except for that inconvenience, it has few side effects. If you think the wholesale cost of Biktarvy is high, don't be surprised by this drug's stratospheric cost—more than $100,000 per year. Alone, it will not stop HIV from advancing. For long-term benefit, it must be co-administered with at least one other drug that the person is susceptible to.

ACTIVIST BRIDGETTE PICOU SAYS: Ibalizumab, better known as Trogarzo, is an entry inhibitor medication for people who have tried and failed multiple classes of HIV medication and cannot achieve viral suppression. It is a monoclonal antibody, which basically means it's engineered to mimic your body's immune system. It is not metabolized in the liver or excreted by the kidney, cutting down on those side effects. Trogarzo binds to a different CD4 cell receptor than other entry inhibitors and interferes with cell-to-cell fusion preventing virus entry. This medication is delivered via intravenous (IV) infusion every two weeks. You will continue to take your current ART regimen as it is not intended to be used alone or to replace it, but to enhance it. The infusions are usually done in office but may be arranged at home as well. Discuss scheduling with your provider as adherence is important to success.

As a biologic, IBA is the first HIV medication made from cells rather than from chemicals. This does not make ibalizumab better, just different. All monoclonal antibodies (or mAbs, hence the last syllable of "ibalizumab"), are made this way, including biologics used to treat rheumatoid arthritis and psoriasis. Ibalizumab 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. Ibalizumab works against both CCR5 and CXCR4 virus, and appears to be synergistic with all other classes of antiretrovirals. Resistance test results revealed no evidence of cross-resistance between Trogarzo and any of the approved classes of HIV drugs. Ibalizumab is widely considered to be an HIV entry inhibitor medication. IBA 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, ibalizumab has the potential to be exposed to the developing fetus.

TheraPatientSupport can assist with your private or government insurance coverage, including AIDS Drug Assistance Program (ADAP) and will also assist in applying any eligible co-pay assistance. Thera Patient Support: (833) 23-THERA (833-238-4372), therapatientsupport.com.

MANUFACTURER

TaiMed USA
DISTRIBUTED BY
Theratechnologies Inc.
theratech.com
trogarzo.com

AVERAGE WHOLESALE PRICE

$2,724.00 per box (2 vials); 10 vials for loading dose and four vials for continuing dose (every two weeks)

PHOTO UNAVAILABLE

INVESTIGATIONAL DRUG AT PRESS TIME

fostemsavir FTR

AI ENTRY/ATTACHMENT INHIBITOR: gp120 ATTACHMENT INHIBITOR

● DHHS RECOMMENDATION NOT YET ESTABLISHED

STANDARD DOSE

Investigational drug at press time. In clinical trials, the investigational dose taken forward for further study was 600 mg twice daily without regard to food. Doses were taken after eating. Must be taken in combination with another antiretroviral(s).

Recommended for heavily treatment-experienced patients with history of three-class antiretroviral resistance in addition to an optimized background regimen of other active antiretroviral drugs. Not studied in treatment-naïve patients. No data in pregnant women or pediatric patients under age 18 years.

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

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

POTENTIAL SIDE EFFECTS AND TOXICITY

A safety analysis of the Phase 3 BRIGHTE study at Week 96 found that 94% of participants experienced at least one side effect during this Phase 3 study, though most were mild in severity. Moderate to severe side effects occurred in 21% of participants and included nausea, diarrhea, headache, immune reconstitution inflammatory syndrome (IRIS), vomiting, fatigue, and weakness or lack of energy. Twelve participants had serious side effects that were related to treatment with fostemsavir, and seven percent of participants had side effects that caused them to leave the study.

POTENTIAL DRUG INTERACTIONS

New interactions continue to be discovered after drug approval. Dose modification of fostemsavir is not required when co-administering with tenofovir DF, ritonavir-boosted atazanavir, ritonavir-boosted darunavir with or without etravirine, etravirine alone, ritonavir alone, or raltegravir + tenofovir DF. Dose modification is also not required when co-administering with rifabutin (with or without ritonavir). It is not recommended to co-administer with rifampin due to significantly reduced levels of fostemsavir. Based on fostemsavir's metabolism, a theoretical interaction likely exists with statins (drugs used to treat high cholesterol). This may require a dose reduction or adjustment of certain statins when co-administered with fostemsavir. No dose modification necessary when co-administered with methadone or buprenorphine. Fostemsavir could affect oral contraceptive concentrations, especially those containing ethinyl estradiol. If a booster is not given in the regimen with fostemsavir, it may be co-administered with a combined oral contraceptive containing norethindrone and 30 mcg or less of ethinyl estradiol. 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.

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MORE INFORMATION

Fostemsavir was submitted for FDA approval in December 2019. It is the first HIV drug of its type to get this far in development. It's a gp120 attachment inhibitor. (That's under the drug class of HIV entry inhibitors.) Watch a video of its mechanism of action at youtu.be/WnreXE-TVi8. Fostemsavir works on the gp120 protein that lies on the surface of human immune cells. It's a necessary part of getting the virus to enter the cell. Fostemsavir prevents attachment to the CD4 immune cell by binding to the CD4 receptor binding sites on gp120 on the virus. This causes the virus to accumulate in extracellular space and is subsequently removed by the body's immune system. Very cool. Fostemsavir is likely to be approved as an oral twice-daily drug, making it unlikely to be used in treatment-naïve individuals. The drug is designed to be used in HIV treatment-experienced people, who typically have fewer options for HIV treatment than those just beginning antiretroviral therapy. An option for treatment-experienced individuals is a good thing. "Even in the era of modern HAART [highly active antiretroviral therapy], antiretroviral (ARV) failure and resistance is still a problem worldwide," wrote HIV specialist Dr. Pedro Cahn and colleagues in *Current Opinion in HIV and AIDS* published in July 2018. Dr. Cahn worked on fostemsavir research. Given that fostemsavir does not appear to have cross-resistance to any currently approved antiretroviral as well as its activity regardless of HIV tropism makes it a welcome new drug for patients with very limited treatment options. Fostemsavir is active against CCR5, CXCR4, and dual-mixed virus (Selzentry is only active against CCR5). An advantage of the HIV entry inhibitors has been to help create an optimized regimen for people needing a new drug. In the Phase 3 BRIGHTE study with fostemsavir, study participants all started the trial with treatment failure on the HIV regimen they were taking at the time of entry into the trial. They were heavily treatment experienced with multidrug resistance. Unfortunately, more treatment experience tends to lead to a less likely chance of therapy success later on down the line. This is why medical providers ask HIV patients to take their meds as best they can. According to results reported in October 2018, the people in BRIGHTE who were able to add one or two other new drugs to their regimen along with the fostemsavir (called an "optimized background therapy," or OBT), did better than those who only had fostemsavir as a new option. For the OBT group, 54% experienced undetectable viral load at one year of treatment (146 of the 272 OBT participants). For the group just adding fostemsavir, because there was nothing else available that they *could* add, 38% reached undetectable viral load. This was highly clinically significant for these patients.

DR. ROSS SLOTTEN SAYS: Fostemsavir, a new agent developed by ViiV, a division of GSK, is a unique class of medication that works by preventing the envelope of HIV from attaching to its receptor on the CD4 (T helper) cell. Unlike entry inhibitors such as maraviroc (Selzentry), the tropism of the virus is unimportant. The medication is taken orally twice daily and must be combined with one or more medications to be effective. The results of a Phase III study known as the BRIGHTE trial were presented at the International AIDS Society meeting in Mexico City in July 2019. Study participants were heavily pretreated and resistant to three classes of HIV medications but were still sensitive to at least one other class of medication. After 96 weeks, 60% of participants were maximally suppressed to less than 40 copies. The most common side effects were nausea and diarrhea, which were mild. Once again, this is a niche drug, designed specifically for those individuals who have failed most other therapies. Unless it can be combined into a once-daily tablet or be given as an injectable agent monthly, yearly, or whatever, it will never be a first-line treatment for HIV infection. Resistance to fostemsavir occurs, so noncompliant people living with HIV will fail a fostemsavir-containing regimen also.

ACTIVIST BRIDGETTE PICOU SAYS: Fostemsavir works by binding to a specific protein called gp120 on the virus, blocking it and thereby prohibiting it from attaching to the CD4 cell. It is a prodrug as opposed to an HIV medication itself. For patients with very resistant HIV it is a fresh way to fight the virus, but is not intended for patients newly starting therapy or those who have achieved viral suppression through regular ART treatment. Since the gp120 protein is common between HIV strains, there is a high barrier to resistance.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com
(877) 844-8872

AVERAGE WHOLESALE PRICE

Not yet established.

INVESTIGATIONAL DRUG AT PRESS TIME

PHOTO UNAVAILABLE

leronlimab PRO 140

EI LONG-ACTING ENTRY/ATTACHMENT INHIBITOR
ENTRY INHIBITOR: CCR5 ANTAGONIST

DHHS RECOMMENDATION NOT YET ESTABLISHED

STANDARD DOSE

One weekly subcutaneous (under the skin) injection of 350 mg used in clinical trials.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

In general, no treatment-related serious side effects have been reported and injection site reactions that occurred during studies have been mostly mild and self-resolving. The most common adverse reactions associated with either placebo or leronlimab included diarrhea, headache, swollen lymph nodes, and high blood pressure. Administration-site reactions occurring in more than 5% of participants were induration (hardening or thickening of the skin), pain, and irritation.

POTENTIAL DRUG INTERACTIONS

Drug-drug interactions associated with leronlimab are currently unknown. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not.

MORE INFORMATION

Leronlimab received FDA Fast Track designation in May of last year. The approval is given to investigational medications for serious or life-threatening conditions and which meet an unmet need. Leronlimab is being studied as part of an HIV drug combination for people with multi-drug resistant virus. Leronlimab is also being studied as a single-drug maintenance therapy for people who have achieved undetectable viral load on a stable HIV regimen. The company developing the drug, CytoDyn, reported no drug resistance observed in people taking leronlimab for up to four years. A tropism test is needed to determine if this medication will work for you. Results of a phenotypic tropism test may take up to a month to complete. Genotypic tests are also available and may provide a faster and less expensive alternative. Leronlimab targets 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). Leronlimab blocks CCR5, a receptor on the outside of a CD4 cell, and shuts down this point of entry for the virus. Most people are infected with R5 virus initially, and then over time, X4 and mixed viruses may predominate. Leronlimab is an immunoglobulin (also called an antibody). The injections can be self-administered. The company developing this drug, CytoDyn, is also studying it for cancer treatment. For a short YouTube video on the drug's mechanism of action, GO TO youtube.com/watch?v=sCMwoVYeRA0.

MANUFACTURER

CytoDyn, Inc.
cytodyn.com

AVERAGE WHOLESALE PRICE

Not yet established.

DR. ROSS SLOTTEN SAYS: Leronlimab is a CCR5 inhibitor currently in Phase 2/3 trials, so it has not yet been approved by the FDA for clinical use. Like maraviroc (Selzentry), it can only be prescribed to individuals with a CCR5-tropic virus, and it is intended as an alternative agent in the setting of resistance to other entry and fusion inhibitors. Leronlimab is also being tested for safety and efficacy as a single agent (monotherapy) against HIV, once undetectability has been achieved in combination with other anti-retroviral medications. In my view, its main drawback is that it must be given as a subcutaneous injection, like the ill-fated Fuzeon. So far, side effects noted have been diarrhea, headache, swollen lymph nodes, and high blood pressure, which will not necessarily pose limitations on its use, unless those side effects are common. One study reported that 65.4% of participants experienced at least one side effect, but only one participant dropped out because of side effects. That study was small and included only 52 people. Injection site reactions were said to be mild and temporary. Perhaps if this medication could be given orally as monotherapy, I might barnstorm for it. Otherwise, it's not a breakthrough and will be yet another niche agent.

ACTIVIST BRIDGETTE PICOU SAYS: Still in investigational studies, leronlimab, also known as PRO 140 in trials, is an HIV drug (CCR5 antagonist) whose mechanism of action is to attach to the CD4 cell receptor and block it, preventing entry of the HIV virus. Leronlimab is also unique as it is intended to be used as monotherapy without the use of other HIV meds. It is an injectable medication given subcutaneously once a week and intended for those with multi-drug-resistant strains of virus.

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DINING OUT FOR LIFE

SUBARU Loves to Care

Egrifta SV

tesamorelin for injection

NON-HIV

INJECTABLE FOR TREATING HIV-RELATED HARD BELLY FAT (LIPOHYPERTROPHY)

STANDARD DOSE

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

A potential complication of HIV, antiretroviral therapy, or growth hormone (GH) deficiency may cause a fat redistribution of adipose tissue, known as lipohypertrophy (a form of lipodystrophy). Previous reports of lipohypertrophy prevalence in the U.S. varied widely, anywhere from 2–60% of all patients with HIV. Abdominal lipohypertrophy is defined by an accumulation of excess abdominal (visceral) adipose tissue (VAT, also called "hard belly") surrounding all abdominal organs (liver, stomach, and pancreas, etc.). Hard belly is a different type of fat (hard fat) compared to subcutaneous fat (regular, or soft, fat). Untreated hard belly (excess visceral/abdominal fat) is linked with serious health issues like cardiovascular disease and/or diabetes, increased mortality risk, or may make it hard to perform certain daily activities.

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

Unlike growth hormone products, Egrifta SV is an analogue of human growth hormone-releasing factor (GRF), which stimulates the pituitary gland to produce and secrete the body's own growth hormone. Egrifta SV reduces VAT while preserving subcutaneous fat. The effect of this agent appears to be greatest within the first three to six months of initiation.

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

Egrifta SV should not be administered to patients who have pituitary gland tumor, surgery, or other pituitary gland problems; active cancer; hypersensitivity to either tesamorelin or ingredients in tesamorelin; who are pregnant or become pregnant; or are less than 18 years old. Egrifta SV should be used with caution in patients who have a history of cancer, problems with blood sugar or diabetes, have scheduled heart or stomach surgery, have breathing problems, are breastfeeding or plan to breastfeed, or taking any other prescription and non-prescription medicines, vitamins, or herbal supplements.

The most common side effects include pain in legs and arms and muscle pain. Other warnings include increased risk of cancer reactivation, insulin-like growth factor-1 (IGF-1), fluid retention, glucose intolerance or diabetes, hypersensitivity reactions, injection site reactions, and mortality in acute critical illness. In the Phase 3 clinical studies, patients receiving tesamorelin had a higher risk of developing diabetes compared to those on placebo. Despite initial thoughts that tesamorelin may have significant drug-drug interactions with medications that use CYP450 (a liver enzyme) for metabolism, a study in healthy volunteers proved otherwise. The patients need to be monitored for potential interaction. Long-term safety on the heart and the blood vessels is unknown. Each dose necessitates mixing 2 mg vials stored at room temperature with 0.5 mL of sterile water for injection. Do not use Egrifta SV if the solution is discolored, cloudy, or contains visible particles. Once reconstituted, the vial should be rolled gently, not shaken, between the hands for 30 seconds to ensure mixture is a clear, colorless solution and is administered right away. If not used immediately, the reconstituted Egrifta SV should be discarded.

SCAN THIS QR CODE WITH YOUR SMARTPHONE TO VIEW THIS PAGE ONLINE.

CAP & PAP INFO

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

MANUFACTURER

Theratechnologies, Inc.
egrifta.com
Thera Patient Support:
(833) 23-THERA
(833-238-4372)
therapatientsupport.com

AVERAGE WHOLESALE PRICE

$6,360.00 /MONTH

Mytesi

crofelemer

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 adult patients with HIV/AIDS on antiretroviral therapy. Currently, what is typically recommended is for the patient to take medication(s) with food and/or use Imodium (loperamide) for symptomatic diarrhea.

Mytesi approval was based on a randomized, placebo-controlled study of 374 HIV-positive patients who had about 3 watery stools per day and were on anti-HIV medicines. At study entry, patients experienced an average of approximately 20 watery stools per week. To be considered a responder, watery stools had to be decreased to two or fewer per week, which occurred in 18% of Mytesi-treated patients vs. 8% of placebo-treated patients at 4 weeks. In an open label extension phase of the study, about 50% of the patients reported two or fewer watery stools per week at 3 months, an effect which was maintained until study end at 6 months. These findings suggest that it may take some time to achieve the optimal effect. Mytesi appears to work best in those who have tried and failed non-prescription anti-diarrheals, have had diarrhea for more than two years, have more than two watery bowel movements per day, and whose bowel movements tend to be "pourable" (not clumpy). Mytesi was less effective in African Americans in this clinical study.

An infectious cause should be ruled out prior to initiating Mytesi. In the placebo-controlled part of the study, side effects were comparable to placebo. The most commonly reported side effect was upper respiratory tract infection (Mytesi, 3.8% of patients vs. placebo, 2.9%). Other reported side effects included bronchitis, cough, flatulence (gas), and increased bilirubin. Based on animal data, Mytesi may cause fetal harm. Mytesi has not been studied in patients younger than 18 years old. Its usefulness in pediatrics is unknown and use in this population cannot be recommended at this time.

There were no significant drug interactions in participants in the clinical study. There was little or no change in CD4 counts and viral load throughout the study.

In a review article in *Expert Review of Clinical Pharmacology* published in 2015 by Castro *et al.*, the use of Mytesi is recommended as a reasonable choice in patients not responding to over-the-counter psyllium and loperamide. Patients should be informed that the benefits of Mytesi are not immediate, possibly taking about four weeks, and if an inadequate response is seen after three months, Mytesi should be discontinued.

SCAN THIS QR CODE WITH YOUR SMARTPHONE TO VIEW THIS PAGE ONLINE.

CAP & PAP INFO

CO-PAY PROGRAM:
(877) 336-4397
Pay no more than $25, maximum benefit of $100 on each prescription.
PAP: (888) 527-6276;
mytesi.com

MANUFACTURER

Napo Pharmaceuticals
mytesi.com
(844) 722-8256

AVERAGE WHOLESALE PRICE

$802.22/60 tablets

Serostim somatropin for injection

NON-HIV INJECTABLE HUMAN GROWTH HORMONE USED FOR TREATING HIV-ASSOCIATED WASTING IN THOSE 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, patients must be taking 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 (requiring 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 visual changes, headache, nausea, or vomiting). Serostim should be avoided in patients who are acutely ill, have an active cancer, or have diabetic retinopathy (damage to one or both retinas). Since HIV-positive patients may have an increased risk of developing new tumors, including from birthmarks or other moles, risks versus benefits of starting Serostim should always be discussed with your provider. Additionally, patients with known malignancies should be carefully monitored, because Serostim may cause increased growth or malignant changes.

Rotate injection sites to avoid injection site reactions. An injection training program is available; see the website or call the toll-free number. 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, there are some potential drug-drug interactions, though no formal drug studies have been conducted. These theoretically potential interactions include patients 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 like 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 INFO

If someone is having difficulty paying for Serostim, there are several programs that may be able to assist the patient with acquiring it. These programs include 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 for additional information.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

6 mg: 7 injections (usually a one-week supply) **$4,576.82**

SCAN THIS QR CODE WITH YOUR SMARTPHONE TO VIEW THIS PAGE ONLINE.

Descovy for PrEP

FTC/TAF
emtricitabine/tenofovir alafenamide

PrEP (PRE-EXPOSURE PROPHYLAXIS)

★ 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 individuals vulnerable to HIV through receptive vaginal sex. Take one tablet once daily, without regard to food. The tablet contains 200 mg emtricitabine and 25 mg tenofovir alafenamide.

Take a missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. Descovy for PrEP is not recommended if CrCl is between 15 to less than 30 mL/min or under 15 if you are not on dialysis.

➤ SEE EMTRIVA, which is contained in Descovy.

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

POTENTIAL SIDE EFFECTS AND TOXICITY

The most common adverse event is diarrhea, observed in up to 5% of individuals given Descovy in the large DISCOVER study that led the FDA to approve Descovy for PrEP. There was also nausea (4%) and headache, fatigue, and abdominal pain (2% each). If Descovy is discontinued abruptly in people with hepatitis B virus (HBV), flare-up of hepatitis may occur—talk to your provider before discontinuing. Check for hepatitis B before taking Descovy and vaccinate against it if appropriate. Drug resistance to HIV therapy may develop if people going on Descovy for PrEP unknowingly already have HIV, or if infection occurs after starting PrEP. However, drug resistance was rare in the extremely few individuals who acquired HIV during the DISCOVER trial (seven out of 2,670 persons on Descovy and 15 out of 2,665 on Truvada). All were in the Truvada arm and all were in those with baseline HIV infections. As with previous PrEP studies, DISCOVER found the effectiveness of Descovy for PrEP was related to drug adherence—taking Descovy 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 who are still growing their bone structure and older individuals who may be becoming frail. Kidney changes may be of greater concern for individuals who have pre-existing kidney problems or older individuals at risk for developing kidney problems. Stigma remains a significant concern of HIV prevention, especially PrEP.

POTENTIAL DRUG INTERACTIONS

Do not take with any other HIV or HBV drugs 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 like 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 became the second FDA approved drug on the market for HIV prevention (called pre-exposure prophylaxis, or PrEP) in October 2019, with one important exception. The FDA specified that Descovy PrEP was not approved for individuals vulnerable to HIV through receptive vaginal sex. This is because the effectiveness of Descovy PrEP was not evaluated in this context. Studies with women and adolescent girls are underway. The tenofovir alafenamide (TAF) in Descovy and the tenofovir disoproxil fumarate (TDF) in Truvada (the first PrEP medication on the market) work differently in the body, raising questions for PrEP, but are both highly effective against the virus whether for treatment or prevention. In the meantime, Truvada, which is basically an earlier version of Descovy, is indicated for PrEP against HIV for all populations, including for use in receptive vaginal sex. Descovy for PrEP was only studied in men who have sex with men (MSM) and transgender women (5,387 MSM and 74 transwomen) in the DISCOVER study that brought Descovy PrEP to market. TAF has less of a negative effect on renal function and bone mineral density than TDF, but the long-term clinical significance of the changes seen with the two medications remains unknown. Medical providers, however, prefer TAF over TDF for certain patients who may be at higher risk for renal and bone toxicity (including youths and older individuals). There are considerations for using PrEP even with U=U (Undetectable equals Untransmittable). A guide to help providers bill for PrEP services is available at nastad.org/resource/billing-coding-guide-hiv-prevention. Two excellent websites for finding a PrEP provider are preplocator.org and aidsvu.org—although any provider can prescribe PrEP. For more information, GO TO cdc.gov/hiv/basics/prep.html.

DR. ROSS SLOTTEN SAYS: "PrEP" stands for pre-exposure prophylaxis against HIV. It has become one of the two cornerstones of HIV eradication, the other being anti-HIV therapy itself. Public health authorities estimate that there are 1.2 million people at risk of HIV in the United States, but less than 100,000 people are taking PrEP. In healthy individuals at risk for HIV, Truvada and Descovy are very safe and the benefits far outweigh the risks. There are few long-term safety data for TAF-containing regimens, although 4 out of 10 patients in one study who were switched from TDF to TAF showed improvement in kidney function. People most at risk for side effects are those who are elderly, have a low body weight, have underlying kidney disease before starting medication or are diabetic, have uncontrolled high blood pressure, or are co-infected with hepatitis C. The bottom line is that for most people PrEP is safe, effective, and easy to take. Careful monitoring of kidney function will pick up problems before they become irreversible. Both drugs are well tolerated. If taken daily, they are 92–99% effective at preventing HIV. Both Truvada and Descovy take 7 days to become fully protective [for anal sex; 21 days for receptive vaginal sex]. It is therefore not recommended to skip doses or take the medication in an unconventional way, like one day before an unsafe sexual contact and a few days afterward, as some have advocated. I don't believe there's solid scientific evidence to back them up yet. If you want to stop PrEP, you should continue to take it for four weeks after the last [condomless] sexual contact. And neither drug protects against other sexually transmitted infections. In the pipeline are a good number of other possible PrEP candidates, including injectable agents, medication implants, vaginal rings embedded with a PrEP agent, etc.

ACTIVIST BRIDGETTE PICOU SAYS: Descovy recently got its approval for pre-exposure prophylaxis (PrEP) use on October 2019. Descovy uses tenofovir alafenamide, instead of tenofovir disoproxil fumarate like in Truvada. This means not only is less medication needed to be effective, it is a smaller pill as compared to Truvada. Also in comparison to Truvada it causes less loss of bone density and kidney toxicity. Descovy was only studied for the MSM and trans women populations. This excludes individuals at risk via receptive vaginal sex. This population will need to continue to use Truvada for PrEP. You need to take Descovy daily to ensure effectiveness. You will be monitored at three-month intervals including HIV and STI testing, and monitoring of your liver and kidney functions.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$2,010.95/month

Truvada for PrEP

FTC/TDF
emtricitabine/tenofovir DF

PrEP (PRE-EXPOSURE PROPHYLAXIS)

★ FDA APPROVED FOR THE PREVENTION OF HIV

STANDARD DOSE

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

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

- **SEE THE INDIVIDUAL DRUGS CONTAINED IN TRUVADA:** Viread and Emtriva
- **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

No new serious side effects were observed when Truvada was studied for HIV prevention in clinical trials. Some patients may experience nausea, headache, stomach pain, or weight loss. Risk compensation (when people put themselves at greater risk for infection, such as anonymous or multiple sex partners, because they think PrEP will protect them) was not observed in clinical trials. The tenofovir DF (Viread) in Truvada is associated with long-term decreases in bone mineral density (BMD). BMD monitoring should be considered in people who have a history of bone fracture due to a disease or are at risk for osteopenia or osteoporosis. Truvada can cause kidney toxicities. In prevention studies, decreases in BMD and creatinine clearance or eGFR (a marker of kidney function) were rare, mild, and usually reversible upon stopping Truvada. 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 kidney or bone problems. If Truvada is discontinued abruptly in people with hepatitis B virus (HBV), flare-up of hepatitis may occur—talk to your provider before discontinuing. In studies, there were cases of people who had unidentified HIV infection when starting Truvada for PrEP and subsequently developed drug resistance. A negative HIV test must be confirmed immediately prior to starting Truvada for PrEP. Truvada alone is not a complete regimen to treat HIV. Continuing only with Truvada after acquiring HIV may lead to drug resistance and limit future antiviral options. Truvada contains lactose, which can cause some abdominal discomfort, especially in patients sensitive to lactose.

POTENTIAL DRUG INTERACTIONS

Do not take with any other HIV or HBV drugs when used 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

A new PrEP drug was approved in October 2019—see Descovy for PrEP page. Truvada for PrEP is almost 100% effective in preventing HIV. 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 be vulnerable 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 people at risk include those who engage in sexual activity in a high-prevalence area or social network and have one or more of the following: (a) inconsistent or no condom use, (b) diagnosis of sexually transmitted infections (STIs), (c) exchange of sex for commodities (money, food, shelter, or drugs), (d) use of illicit drugs or alcohol dependence, (e) history of incarceration, or (f) sexual partners of unknown HIV status with any of the above risk factors. Screening and monitoring requirements include checking for STIs and hepatitis B and C. The National Alliance of State and Territorial AIDS Directors (NASTAD) developed a guide to help providers bill for PrEP services available at nastad.org/resource/billing-coding-guide-hiv-prevention. Two excellent websites for finding a PrEP provider are preplocator.org and aidsvu.org—although any provider can prescribe PrEP. Gilead Sciences helps patients work with their insurance, including pre-authorizations, as well as provides free PrEP to uninsured patients who are eligible and co-pay assistance up to $7,200 a year; contact the patient assistance hotline at (877) 505-6986, or GO TO gileadadvancingaccess.com. PrEP Facts: Rethinking HIV Prevention and Sex is a closed Facebook group for people interested in or currently on PrEP, and their allies. For more information, GO TO cdc.gov/hiv/basics/prep.html.

DR. ROSS SLOTTEN SAYS: "PrEP" stands for pre-exposure prophylaxis against HIV. It has become one of the two cornerstones of HIV eradication, the other being anti-HIV therapy itself. Public health authorities estimate that there are 1.2 million people at risk of HIV in the United States, but less than 100,000 people are taking PrEP. Truvada and Descovy are similar drugs manufactured by Gilead Sciences, Inc. The difference is that Truvada contains tenofovir disoproxil fumarate (TDF) and Descovy, tenofovir alafenamide (TAF). In healthy individuals at risk for HIV, Truvada and Descovy are very safe and the benefits far outweigh the risks. In a 4-year follow up of 10,343 individuals on a TDF-containing regimen, serious events occurred in 0.5% of that cohort. In 2.2% of study subjects, serum creatinine levels increased by 0.5 mg/dL (an increase considered to be significant). There are few long-term safety data for TAF containing regimens, although 4/10 patients in one study who were switched from TDF to TAF showed improvement in kidney function. People most at risk for side effects are those who are elderly, have a low body weight, have underlying kidney disease before starting medication or are diabetic, have uncontrolled high blood pressure, or are co-infected with hepatitis C. The bottom line is that for most people PrEP is safe, effective, and easy to take. Careful monitoring of kidney function will pick up problems before they become irreversible. Both drugs are well tolerated. If taken daily, they are 92–99% effective at preventing HIV. Both Truvada and Descovy take 7 days to become fully protective [for anal sex; 21 days for receptive vaginal sex]. It is therefore not recommended to skip doses or take the medication in an unconventional way, like one day before an unsafe sexual contact and a few days afterward, as some have advocated. I don't believe there's solid scientific evidence to back them up yet. If you want to stop PrEP, you should continue to take it for four weeks after the last [condomless] sexual contact. And neither Truvada nor Descovy protects against other sexually transmitted infections. In the pipeline are a good number of other possible PrEP candidates, including injectable agents, medication implants, vaginal rings embedded with a PrEP agent, etc.

ACTIVIST BRIDGETTE PICOU SAYS: Approved in 2012, Truvada for PrEP was a welcome addition in the fight against HIV. PrEP is pre-exposure prophylaxis. Taken once daily, the simple dosing offers 92- 99% effectiveness. It is mostly well tolerated with the most common complaints being stomach upset and headache. Current guidelines call for three month interval testing for HIV status, STIs, and kidney and liver function. Truvada has been known to cause loss of bone density and kidney toxicity, so keep an eye on that with your healthcare provider. Unlike Descovy, Truvada is indicated for all groups of people at risk for HIV including MSM, people who are transgender, and those who have receptive vaginal sex. While taking PrEP remember to take it each day as directed.

MANUFACTURER

Gilead Sciences, Inc.

gilead.com
truvada.com
(800) GILEAD-5
(445-3235)

AVERAGE WHOLESALE PRICE

$2,010.95/month

CHOICE OPTIONS

DHHS Guidelines for people starting HIV therapy for the first time

DHHS recommends starting antiretroviral therapy (ART) as soon as possible after HIV is diagnosed, regardless of CD4 count. Most people starting HIV treatment for the first time (treatment-naïve) should take one of the following: Biktarvy; Dovato; Triumeq; Tivicay plus Descovy or Truvada; or Isentress HD or Isentress plus Descovy or Truvada. GO TO aidsinfo.nih.gov for more information.

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

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

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
HLA: human leukocyte antigen
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

Recommended initial regimens for most people with HIV

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

INSTI + 2 NRTIs[1]

BIC + FTC + TAF
Biktarvy
A1

DTG + ABC + 3TC
Triumeq
if HLA-B*5701-negative
A1

DTG + FTC + TAF or TDF
Tivicay with **Descovy** or **Truvada**
A1

RAL + FTC + TAF or TDF
Isentress HD or **Isentress** with **Descovy** (B2) or **Truvada** (B1)

INSTI + 1 NRTI

DTG + 3TC
Dovato[2]
A1

Recommended initial regimens in certain clinical situations

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

Boosted PI + 2 NRTIs[1]

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

DRV + c + FTC + TAF
Symtuza
A1

OR

DRV + c + FTC + TAF or TDF
Prezcobix with **Descovy** or **Truvada**
A1

OR

DRV + r + FTC + TAF or TDF
Prezista + **Norvir** with **Descovy or Truvada**
A1

ATV + c + FTC + TAF or TDF
Evotaz with **Descovy** or **Truvada**
B1

OR

ATV + r + FTC + TAF or TDF
Reyataz + **Norvir** with **Descovy or Truvada**
B1

DRV + c + ABC + 3TC
Prezcobix with **Epzicom**
if HLA-B*5701-negative
B2

OR

DRV + r + ABC + 3TC
Prezista + **Norvir** with **Epzicom**
if HLA-B*5701-negative
B2

Recommended initial regimens in certain clinical situations (CONTINUED)

NNRTI + 2 NRTIs[1]

DOR 3TC TDF
Delstrigo
B1

OR

DOR FTC TAF
Pifeltro with **Descovy**
B3

EFV 600mg FTC OR 3TC TDF
Atripla or **Symfi**
B1

OR

EFV 400mg 3TC TDF
Symfi Lo
B1

OR

EFV 600mg FTC TAF
Sustiva with **Descovy**
B2

RPV FTC TAF OR TDF
Odefsey or **Complera**
if viral load <100,000 copies/mL and CD4 count >200 cells/mm^3
B1

INSTI + 2 NRTIs

EVG c FTC TAF OR TDF
Genvoya or **Stribild**
B1

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

DTG 3TC
Dovato[2]
A1

DRV r RAL
Prezista + **Norvir** with **Isentress** (twice daily) if viral load <100,000 copies/mL and CD4 count >200 cells/mm^3
C1

DRV r 3TC
Prezista + **Norvir** with **lamivudine**[1]
C1

NOTE: THE FOLLOWING ARE AVAILABLE AS CO-FORMULATED DRUGS (NOT A COMPLETE LIST)
Cimduo or Temixys: 3TC/TDF
Epzicom: ABC/3TC
Evotaz: ATV/c
Biktarvy: BIC/FTC/TAF
Delstrigo: DOR/3TC/TDF
Prezcobix: DRV/c
Symtuza: DRV/c/FTC/TAF
Dovato: DTG/3TC
Triumeq: DTG/ABC/3TC
Symfi Lo: EFV 400 mg/3TC/TDF
Symfi: EFV 600 mg/3TC/TDF
Atripla: EFV/FTC/TDF
Genvoya: EVG/c/FTC/TAF
Stribild: EVG/c/FTC/TDF
Descovy: FTC/TAF
Truvada: FTC/TDF
Odefsey: RPV/FTC/TAF
Complera: RPV/FTC/TDF

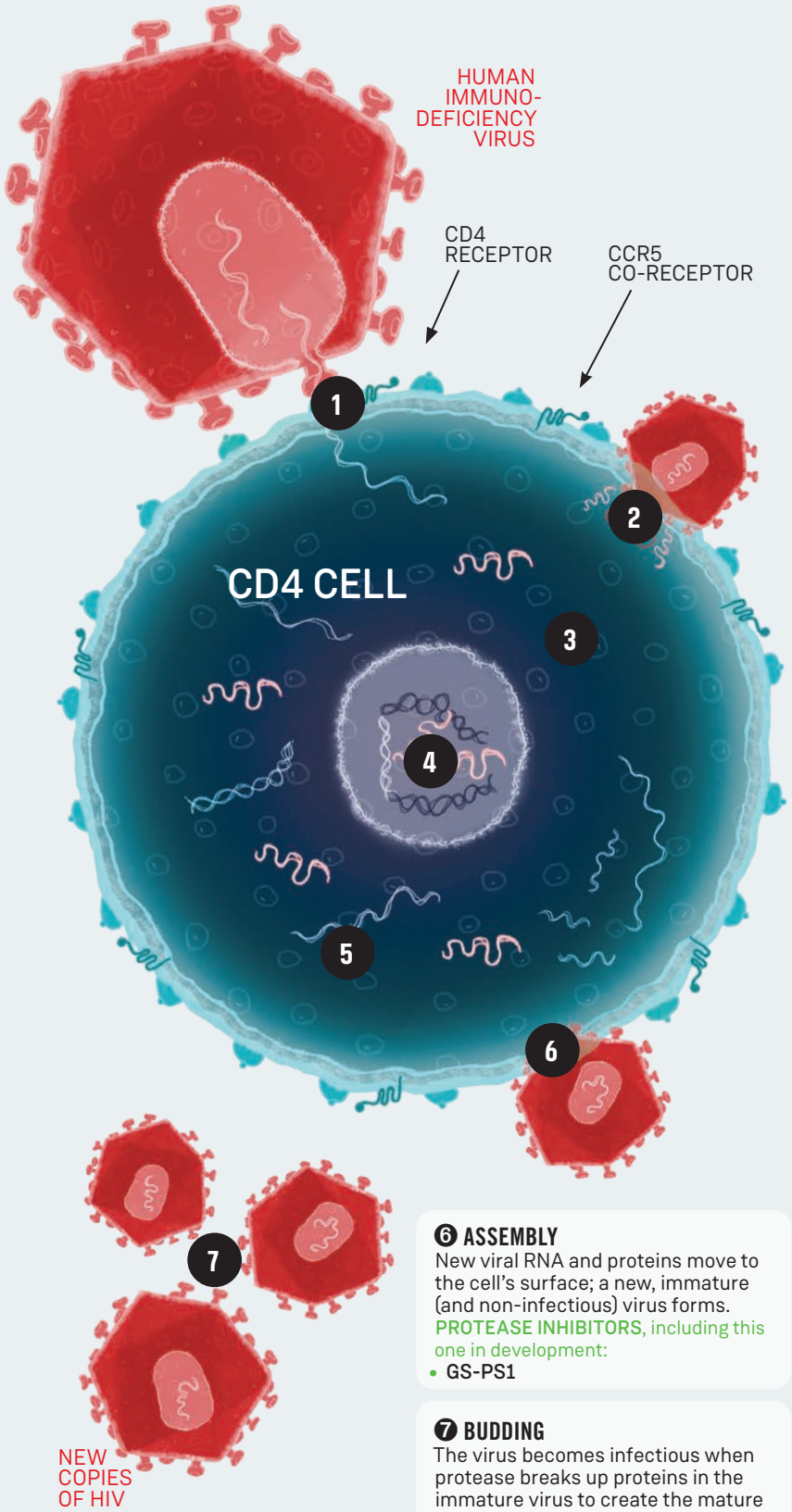
FOOTNOTES
1 **Lamivudine (3TC)** may substitute for emtricitabine (FTC) or vice versa.
2. Except for individuals with pre-treatment HIV RNA greater than 500,000 copies/mL; who are known to have active hepatitis B virus (HBV) coinfection; or who will initiate ART before results of HIV genotype testing for reverse transcriptase or HBV testing are available.

NOTES:
- **Tenofovir alafenamide (TAF)** and **tenofovir disoproxil fumarate (TDF)** are two forms of tenofovir that are approved by the Food and Drug Administration. TAF has fewer bone and kidney toxicities than TDF, while TDF is associated with lower lipid levels. Safety, cost, and access are among the factors to consider when choosing between the two.
- **raltegravir** (RAL) can be given as RAL 400 mg twice daily or RAL 1,200 mg (two 600 mg tablets) once daily.

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 (see next page).



❶ BINDING

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

- **fostemsavir**
- **combinectin**

❷ FUSION

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

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

❸ REVERSE TRANSCRIPTION

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

- **EFdA**
- **GS-9131**

and NNRTIs, including these in development:

- **elsufavirine**
- **rilpivirine LA**

❹ INTEGRATION

Viral DNA is transported into the host cell's nucleus and integrates into the host's DNA.
INTEGRASE INHIBITORS, including these in development:

- **cabotegravir**
- **cabotegravir LA**

❺ REPLICATION

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

❻ ASSEMBLY

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

- **GS-PS1**

❼ BUDDING

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

- **GS-CA1**

and MATURATION INHIBITOR in development:

- **GSK3640254**

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

WHAT'S COOKING?

A sneak peek at some of the new drugs coming soon

AJA KOSKA-ISTOCKPHOTO

ABBREVIATIONS

3TC: lamivudine
bNAb: broadly neutralizing antibody
AZT: zidovudine
FDC: fixed-dose combination
FTC: emtricitabine
INSTI: integrase inhibitor
mAb: monoclonal antibody
NNRTI: non-nucleoside reverse transcriptase inhibitor
NRTI: nucleoside reverse transcriptase inhibitor
PI: protease inhibitor
STR: single-tablet regimen
TAF: tenofovir alafenamide
TDF: tenofovir disoproxil fumarate

Completed Phase 3 study and submitted for approval

cabotegravir
Oral formulation of an integrase inhibitor mainly used for lead-in dose before long-acting formulation. From ViiV.

cabotegravir LA/ rilpivirine LA
An INSTI/NNRTI injection with very long half-life—detectable after more than one year following single injection. CAB LA / RPV LA injection studied for treatment, and CAB LA for prevention as single INSTI injection. From ViiV. See drug page in this guide.

fostemsavir (GSK3684934)
A gp120 attachment inhibitor. 48-week results from the Phase 3 BRIGHTE study in heavily treatment-experienced with extensive drug resistance. From ViiV. See drug page in this guide.

Phase 3

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

UB-421
Monoclonal antibody CD4 binding. Infusion dosed either weekly or every two weeks as alternative to ART during treatment interruption. From United BioPharma.

Phase 1/2

MK-8591 (EFdA)
A new NRTI, highly potent, low dose, active against NRTI resistance. Long half-life, potential as oral (weekly dose) and implant (annual implant for PrEP). From Merck.

MK-8591/3TC/ doravirine
Fixed-dose combination of the NNRTI doravirine plus generic 3TC and new NRTI MK-8591 (EFdA). From Merck.

GS-9131
A new NRTI active against NRTI resistance. Synergy reported with AZT, FTC, abacavir, efavirenz, bictegravir, dolutegravir and lopinavir; additive activity with TDF and TAF. Will be co-formulated with other Gilead drugs. Phase 2 dose-finding study in Ugandan women. From Gilead.

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

3BNC117 and 10-1074; PGDM1400 and PGT121; 10E8, etc. bNAb (broadly neutralizing antibody)
Many other bNAbs are in development, often in dual or triple combination and including trispecific molecules. (See "Scenes from the bNAb Revolution" in Jan + Feb 2020 issue). Potential as switch option without ART and in current studies for use as PrEP.

Phase 1 and pre-clinical

Combinectin (GSK3732394)
A gp41 / CD4 entry inhibitor. Combined adnectin/fusion inhibitor that stops viral entry by targeting multiple sites of action; potential for self-administered once-weekly injections. From ViiV.

GS-PI1
New once-daily unboosted protease inhibitor; high potency, long half-life, potential for fixed-dose combination single-tablet regimen. From Gilead.

GS-CA1
Early stage for a new drug class (capsid inhibitor) with activity at multiple stages of viral lifecycle. Subcutaneous injection with monthly or less frequent dosing. Phase 1 in HIV positive participants is ongoing. From Gilead.

MK-8583, MK-8527, MK-8558
NRTI and other drug class. These three compounds are registered for Phase 1 in HIV positive participants, with limited details on mechanisms of action. They are plausibly likely to have potential to be long-acting. From Merck.

ADAPTED FROM
HIV Pipeline 2019: New Drugs in Development, published by HIV i-Base, July 2019. For the full report, **GO TO** http://i-base.info/hiv-pipeline-report-2019/

Are You Ready to SYNC?

SYNChronicity

The National Conference for HIV, HCV, STI and LGBTQ Health

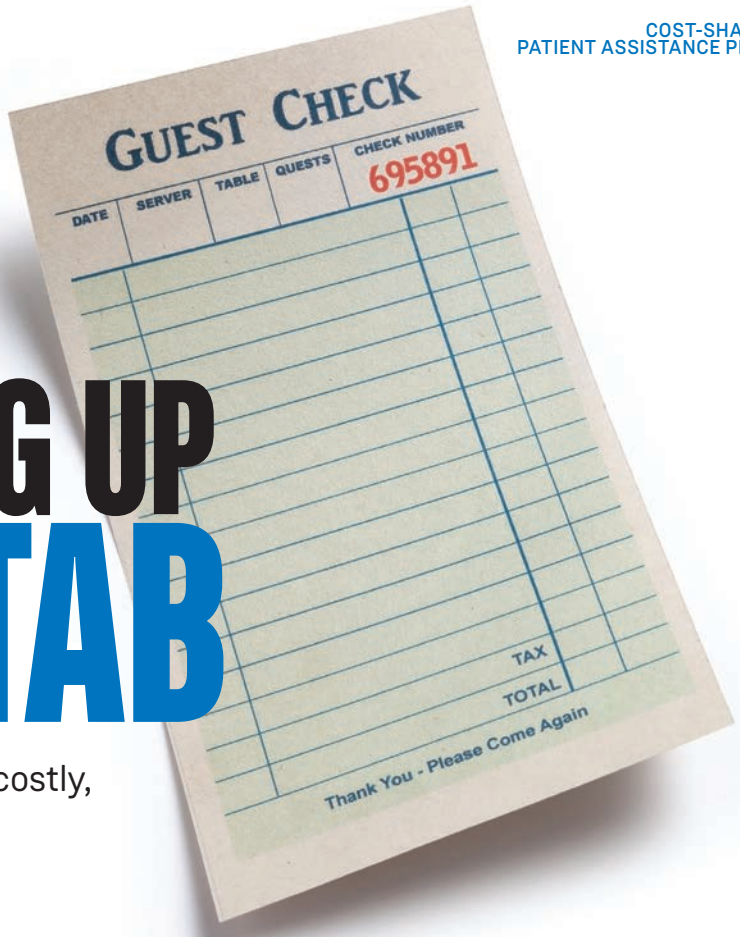
May 10-12, 2020 • Grand Hyatt • Washington, DC

- Over 100 Speakers Addressing HIV, HCV, STI and LGBTQ Health
- Free CME, CNE, CE and CHES Credits
- Four Plenary Sessions
- Eleven Tracks With More Than 40 Sessions
- Half-Day Institutes and Trainings
- Exhibitors and Poster Hall

VISIT

SYNC2020.ORG

FOR AGENDA AND REGISTRATION



PICKING UP THE TAB

HIV treatment can be costly, but there's help

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

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

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

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

Applying for PAPs

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

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

INFORMATION IN THIS ARTICLE and the tables on the following pages are adapted from NASTAD's "HIV Pharmaceutical Company HIV Patient Assistance Programs and Cost-Sharing Assistance Programs": nastad.org/resource/pharmaceutical-company-hiv-patient-assistance-programs-and-cost-sharing-assistance-programs.

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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 the first $400 per prescription per month. **Norvir:** Covers up to $1,200 a year for co-payments.	Renews as long as criteria are met
Temixys	**Celltrion**		
Atripla, **Biktarvy**, **Complera**, **Descovy**, **Emtriva**, **Genvoya**, **Odefsey**, **Stribild**, **Truvada**, **Tybost**, and **Viread**	**Gilead Sciences** 877-505-6986; gileadadvancingaccess.com	**Biktarvy, Descovy, Genvoya, and Truvada:** Covers the first $7,200 per year of co-payments. **Atripla, Complera**, **Odefsey**, and **Stribild:** Covers the first $6,000 per year of co-payments. **Emtriva** and **Viread:** Covers the first $300 per month/$3,600 per year of co-payments. **Tybost:** Covers the first $50 per month/$600 per year of co-payments.	Reapply each year
Edurant, **Intelence**, **Prezista**, **Prezcobix**, and **Symtuza**	**Janssen Therapeutics** 866-836-0114; janssencarepath.org; 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 per year of co-payments, deductibles, and co-insurance for each of 12 eligible prescriptions.	Enrollment is valid until coupon expires, 12/31/2020
Cimduo, **Symfi**, and **Symfi Lo**	**Mylan** 724-514-1800; cimduo.com; symfi.com; symfi-lo.com	**Symfi** and **Symfi Lo:** Covers up to $6,000 annually in out of pocket expenses for prescriptions for those with commercially available insurance. **Cimduo:** Covers up to $4,800 per year.	Reapply each year
Trogarzo	**Theratechnologies** 833-238-4372; trogarzo.com; therapatientsupport.com	Contact program for details	
Dovato, **Juluca**, **Lexiva**, **Rescriptor**, **Retrovir**, **Selzentry**, **Tivicay**, **Triumeq**, **Trizivir**, **Viracept**, and **Ziagen**	**ViiV Healthcare** 844-588-3288; ViiVconnect.com	**Dovato** and **Juluca**, $6,250; **Tivicay**, $5,000; and **Triumeq**, $7,500 per year/per patient maximum. **Lexiva, Rescriptor, Retrovir, Selzentry, Trizivir, Viracept, and Ziagen:** $4,800 per year/per patient maximum.	Automatic renewal
Invirase and **Viread**	**Patient Access Network Foundation** 866-316-7263; panfoundation.org	Maximum benefit is $3,400 per year. Patients may apply for a second grant during their eligibility period subject to availability of funding.	Reapply each year

PATIENT ASSISTANCE PROGRAMS (PAP)

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

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

FOUNDATIONS

PROVIDING ACCESS TO CARE ASSISTANCE FOR PEOPLE LIVING WITH HIV

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

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

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

ADDITIONAL RESOURCES

THESE MAY BE OF INTEREST TO INDIVIDUALS LIVING WITH HIV

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

Fair Pricing Coalition (FPC)
fairpricingcoalition.org
As part of their advocacy work, the Fair Pricing Coalition (FPC) 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.

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.

WHAT'S NEW?

THE LATEST ON SEXUAL TRANSMISSION OF HEP C

BY HEPATITIS C EDITOR **ANDREW REYNOLDS**

IN 2014, I wrote an article titled "Can Hepatitis C be Sexually Transmitted?" with a subhead that answered, "Yes. No. Maybe. It's complicated. All of the above." Fast forward more than five years later and while we have more clarification on sexual transmission of HCV thanks to excellent research on the topic, it can still be pretty complicated. We have consensus that MSM living with HIV are at increased risk of sexual transmission of HCV. We have a clearer picture of risk factors and sexual practices that may enhance the chance of infection, including re-infection of HCV. We are also starting to see warning signs for a potentially newly emerging population at risk of sexual transmission of HCV: More and more examples of HIV-negative MSM on PrEP with no history of injecting drugs. Finally, and most importantly: In 2014, we were at the start of the direct acting antiviral era, in which HCV can be treated and cured without interferon injections, with far fewer side effects and at much higher cure rates. Today, we have come even further, with HCV cure and treatment that is short (8–12 weeks), effective (a cure rate of over 95%) and easy (very few side effects).

This article will provide an update on our current state of knowledge about sexual transmission of HCV in HIV-infected MSM and in HIV-uninfected MSM on PrEP, and close with a list of ways to reduce the chances of getting HCV.

For more information on hepatitis C, what it is, how it's transmitted, tested for and treated, check out the POSITIVELY AWARE Viral Hepatitis Drug Guide: positivelyaware.com/issues/july-august-2019.

HIV and sexual transmission of HCV?

There is consensus that people living with HIV (PLWH) are at risk of sexual transmission of HCV, but it's still not entirely clear why. We know some of the activities and behaviors associated with HCV transmission, and that there are some likely biological reasons, too (see next page). A recent scientific review of sexual transmission of HCV in MSM living with HIV found a prevalence (that is, the percentage of people who acquired HCV) of 8.3%. By comparison, that same study found a prevalence of 1.5% in HIV-negative MSM.

Research has shown that condomless anal sex, group sex, fisting, use of non-injectable drugs (often with sex), are commonly associated with sexual transmission of HCV. Biologically, a review shows that there is a relationship between lower CD4 counts and increased risk of HCV acquisition. Additionally, rates of HCV were higher in HIV-positive gay men with lower CD4 counts even when they had fewer risk factors for HCV. Small studies have also found HCV in the semen and non-bloody rectal fluids of HIV/HCV co-infected MSM, so even in the absence of blood, there could be risk of transmission from sexual fluids.

Regardless of the how it happens, we know that it happens more frequently in people living with HIV; regular testing for HCV, followed by treatment is a great way to stay healthy. Hepatitis C treatment is safe and effective for people living with HIV.

What about HIV-negative MSM who are on PrEP?

We are learning a lot about this, with more and more scientific papers and conference presentations addressing sexual transmission of HCV in MSM taking PrEP, and there is emerging evidence of increased risk for it in this group.

We don't have as much data and information with MSM on PrEP as we do for MSM living with HIV, but there is enough to inform our health education and prevention work. A report looking at 14 case studies of HIV-negative MSM on PrEP who acquired HCV through sex found that, similar to people living with HIV, risk factors such as multiple partners, non-injection drug use, condomless receptive anal sex, and co-occurring STIs were associated with sexual transmission of HCV. Another recent study out of France found new infection rates for HIV-negative MSM on PrEP exactly mirrored the new infection rates of MSM living with HIV, and another recent study out of Amsterdam found higher rates of sexually transmitted HCV in MSM on PrEP.

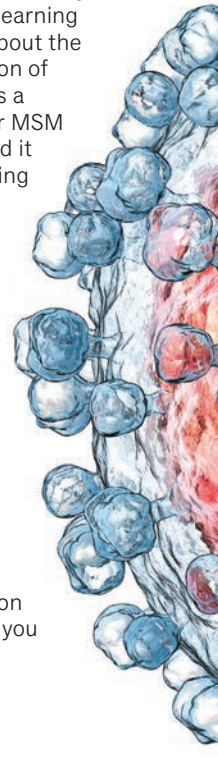
A final thought on HCV risk and PrEP: PrEP is an effective and excellent way to prevent HIV. Overall, the studies referenced here and the number of HCV cases is pretty small compared to the over 90,000 people taking PrEP in the U.S, not to mention all those in Europe who are taking it. It's worth noting that none of the men in the studies referenced above tested positive for HIV, and ultimately, that is what PrEP is: an HIV prevention intervention. In this respect, it is a remarkable success. Routine prevention counseling, screening, and treatment of HCV and STIs are important components of PrEP service delivery.

Screening recommendations for hepatitis C in MSM

Routine HCV screening, followed by treatment for all people is the ideal way to improve both the individual health of the person living with HCV as well to reduce transmission and improve public health. We're not there yet, but in the meantime, testing for HCV—at least annually, and maybe even every six months—is a great way to keep up with your HCV status.

Conclusions

There has been so much progress in both HIV prevention and treatment, and we can eliminate HCV among MSM, too. We're learning more and more about the sexual transmission of HCV: We know it's a significant risk for MSM living with HIV and it may be an emerging concern for HIV-negative MSM on PrEP. As we learn more, we can engage in prevention education and awareness, test for HCV routinely, and get people treated and cured. It's my hope that the next time I write an update about sexual transmission of HCV, it's to tell you that it's gone.



Harm reduction tips to reduce your risk for hepatitis C

1. Test for HCV routinely. Testing for HCV alone is not prevention, but knowing your status so you can seek treatment and prevent transmitting it to others is very important. You should test at least once per year, but might consider more frequent testing depending upon your level of risk..

2. Talk to your partner(s) about hepatitis C. If they are HCV-positive, or they don't know their HCV status, you might consider activities that are less likely to transmit HCV, such as oral sex, masturbation or wearing a condom for anal sex. Communication and awareness of your sex partner's status is especially important if you are sero-sorting and only having sex with other HIV-positive men.

3. Wear a condom for anal sex. Both tops and bottoms are at an increased risk for sexual transmission of HCV. Condoms can provide an effective barrier to prevent blood contact during anal sex. Use water-based lube to make sex smoother and minimize the chance for micro tears and bleeding.

4. Practice safer fisting. As with anal sex, both tops and bottoms are at increased risk for sexual transmission of HCV. Check your hands for any cuts or bleeding cuticles. Wear latex gloves, and change into new, unused ones for each new partner. HCV is a tough virus and can live in water for up to 21 days, so although we may not know how long it can live in lube, it's good practice to not share lube between partners, either.

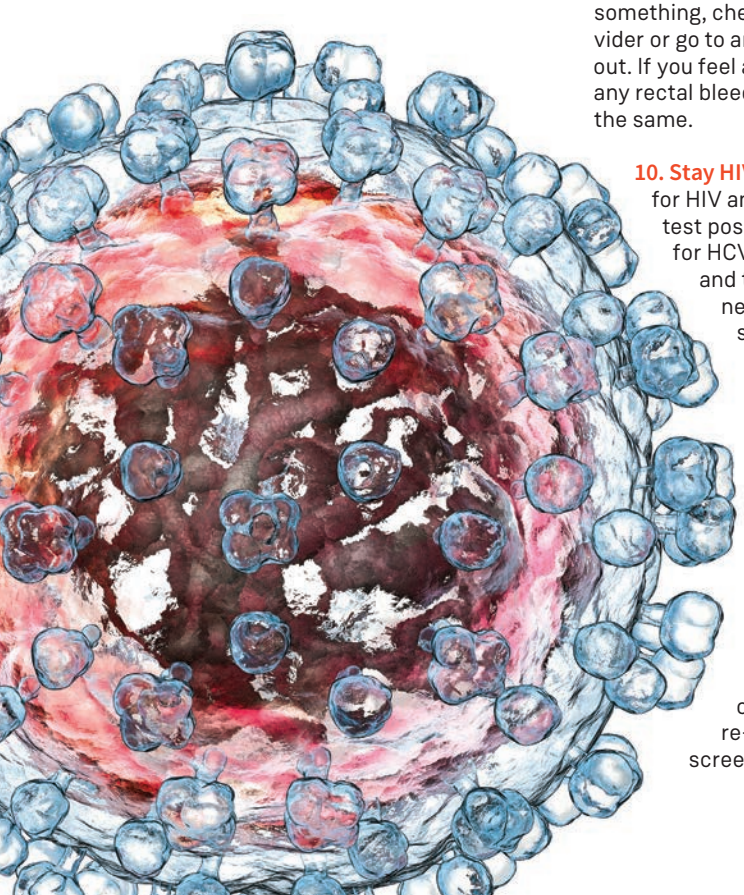
5. Sequence your sex play. Avoid receptive anal sex after fisting or vigorous sex toy play that may have caused tearing and bleeding in the rectum, or you could be the top for anal sex.

6. Keep your sex toys clean. Cover your dildos and vibrators with condoms and change them for new ones with each partner. Do not use toys with more than one person before fully washing them.

7. Take a break from anal play. If you recently had anal warts removed, or had a case of hemorrhoids, take a break from bottoming to give yourself a chance to heal. The same is true following any type of receptive anal sex, especially if you see any blood or feel any discomfort or pain.

8. If you use drugs during sex, don't share anything. Whether you use injectable or non-injectable drugs, don't share anything. HCV can live on surfaces for a very long time in syringes, on surfaces, and in drug using equipment, and anything with HCV-infected blood on it can transmit the virus.

9. Screen for STIs regularly. Routine screenings for STIs that can cause sores—primary syphilis, herpes, anal warts, etc.—are an important part of your sexual health. If you are sexually active, aim for STI testing every 3–6 months. Perform self-exams, too, and check for any sores (especially if you have a history of herpes or anal warts). If you see something, check with your medical provider or go to an STI clinic to get it checked out. If you feel any rectal discomfort or see any rectal bleeding or other discharge, do the same.



10. Stay HIV-negative. Screen routinely for HIV and know your status. If you test positive, get into care, screen for HCV, and talk about HIV care and treatment. If you test HIV negative, continue to practice safer sex and safer drug use, screen for STIs regularly, and talk to your medical provider about PrEP.

BONUS TIP: Get cured of HCV. When you're cured of HCV, you have no virus in your body, and thus no chance of transmitting HCV. "Cure as prevention" is an excellent tool for taking care of both yourself and your sex partners. After getting cured, stay mindful of HCV re-infection and continue to screen for HCV at least annually.

WHAT ACTIVITIES INCREASE THE RISK OF SEXUALLY TRANSMITTED HCV?

Fisting: Fisting can cause trauma to the surfaces of the anus and rectum that could lead to bleeding, including microscopic bleeding. Fisting someone else might also increase your risk if you have breaks in your skin fingers and hands.

Sharing sex toys: As with fisting, sex toys can lead to anal/rectal bleeding. If a sex toy has HCV-infected blood on it, it may facilitate transmission of the virus. Note: There have not yet been any studies examining HCV on sex toys, but we know that HCV can live on surfaces for as long as 16 days, so it's a safe assumption that it can live at least that long on sex toys, and the same caution should be exercised.

Group sex: Engaging in group sex appears to increase the risk of sexual transmission of HCV. This may be due to longer sex sessions that might lead to more trauma and bleeding, but it could also increase the likelihood of coming into contact with someone with HCV.

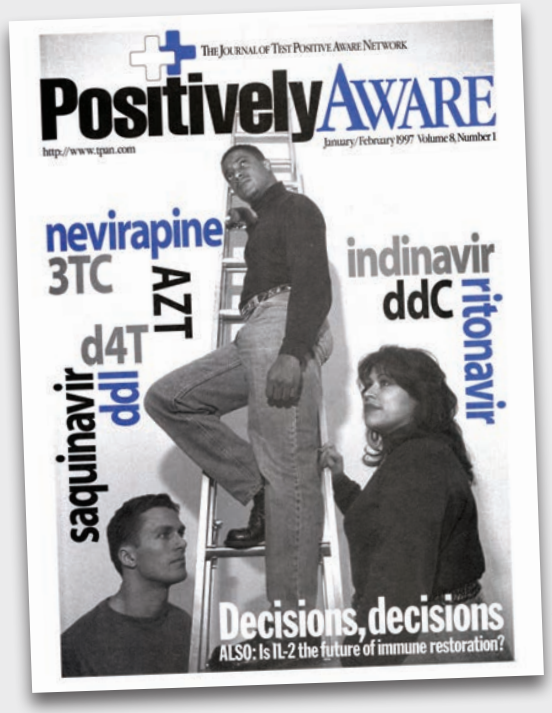
Multiple sex partners: As with group sex, having multiple partners is associated with sexual transmission of HCV: More partners increases the possibility of having sex with someone with HCV, but it has also been shown to coincide with other risk behaviors.

STDs (STIs): Sexually transmitted diseases that cause sores are associated with HCV because of the presence of blood, especially syphilis and herpes. Anal warts, specifically sex following anal wart removal and before sufficient healing, have also been found to increase the risk of HCV.

Using non-injectable drugs with sex: HCV transmission can occur due to the sharing of intranasal straws or pipes, but using substances during sex might also decrease one's inhibitions and lead to more risk taking than usual.

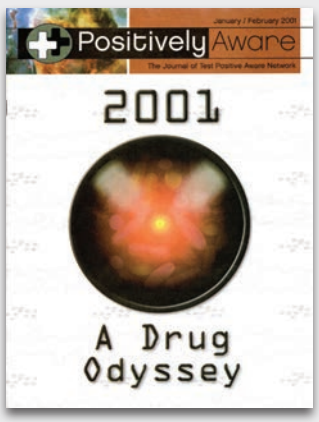
MAKING THE COVER

PA's former and current art directors look back at what inspired them to design the cover of the drug guide



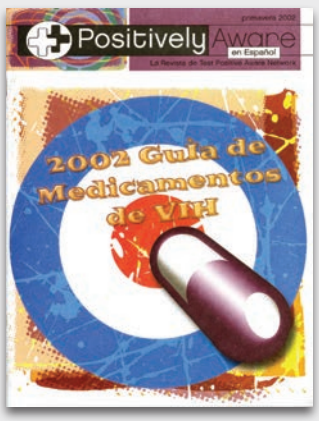
1997: DECISIONS, DECISIONS

With the advent of protease inhibitors—the first effective HIV drugs—people living with HIV now had viable treatment options. The drug guide was the brainchild of then-editor Brett Grodeck. "Nine drugs that specifically fight HIV are approved in the United States as of January 1997," wrote associate editor Enid Vázquez, who has compiled the annual drug guide since the beginning. "There are pros and cons to each drug. POSITIVELY AWARE offers its first guide to HIV therapy." The cover conveyed the new and growing number of treatment options to consider. And as Vázquez noted, "Two of the individuals appearing on this cover were living with HIV—and they're both alive and kicking today."



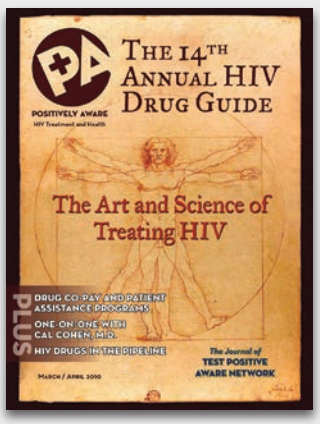
2001: A DRUG ODYSSEY

Russell McGonagle, who served as art director from 1995 to 2010, paid tribute to the Stanley Kubrick classic, *2001: A Space Odyssey.* The ship's computer, HAL, was both caretaker and villain. HIV drugs—seen reflected in HAL's lens—can be very similar, providing positive treatment and sometimes negative side effects in the mission of treating the patient.



2002: GUÍA DE MEDICAMENTOS

For several years we produced quarterly versions of the magazine in Spanish as *Positively Aware en Español.* The 2002 *Guiá de Medicamentos de VIH* was an homage to Pop Art. *Durante varios años producimos versiones trimestrales de la revista en español,* Positively Aware en Español. *El 2002 Guiá de Medicamentos de VIH fue un homenaje a Pop Art.*



2010: THE ART AND SCIENCE OF TREATING HIV

After 12 years, this was McGonagle's final cover. Editor-in-chief Jeff Berry suggested using Leonardo da Vinci's *Vitruvian Man.* Vitruvius was a first century Roman architect who believed that the measurements and proportions of the human body were divinely created, perfect, and correct, symbolizing the merging of art and science.

2011: SINGIN' IN THE RAIN

Into each life a little rain must fall, which made the film *Singin' in the Rain* the inspiration for art director Rick Guasco's first cover. With its sunny smile and optimistic outlook, photographer Chris Knight brought the image to life. Note that the raindrops are meant to be HIV medication.

2016: LIFE IN PANORAMA

It seemed only appropriate that the photo shoot for POSITIVELY AWARE's first ever foldout cover would be staged in Hollywood. Movies are bigger than life. The stories, the characters, the special effects—even the size of a movie screen or this magazine cover—are intended to take up your entire view. Photographer Louis "Kengi" Carr assembled a "cast" of 22 people living with HIV. "Being HIV-positive is just one facet of my life, and it's not a bad thing," said Cathy Elliot, 51, HIV-positive since 1995. "People outside of the HIV community might not understand, but coping with HIV for all these years has made me resilient. I'm a better human being overall. I truly value the relationships that I have with my community, and I celebrate every day as a gift."

2012: FOLLOW THE YELLOW BRICK ROAD

"Life with HIV can be an odd journey," said the article describing the 2012 cover. "You've been uprooted from the life you've known, and suddenly plopped down in the midst of a new set of circumstances. How to convey that on a magazine cover? The answer was obvious: *The Wizard of Oz*." It's all about the yellow brick road, which is made up of HIV meds. The sketch of Dorothy and friends (below) was drawn on a cocktail napkin by illustrator Ursula Martens, and then turned into this cover by Joshua Thorne.

2016: WHERE EVERYONE KNOWS YOUR NAME

After hours one Sunday evening, Slade's Barbershop in Chicago's Boystown neighborhood was taken over for the cover, shot by John Gress. The concept was a familiar gathering spot, inspired by the TV series *Cheers*—for this behind the scenes photo, everyone was instructed to yell, "Norm!"

THE GIFT OF CHOICE

Intergenerational conversations have a power of their own

BY **IAN L. HADDOCK**

AN 18-YEAR-OLD recent graduate of high school, I was sitting at my chosen father's computer desk downloading music. It was 2006 and we had met just a few months before. I was like many young boys just coming out as LGBTQIA+—homeless from severed ties with family associated with my being queer, rebelling against the assumed shame of coming out, having survival sex, being promiscuous out of simply figuring out what I liked sexually and absent of many responsibilities yet with the weight of the world on my shoulder. I had a good head on me, but my potential had been misplaced by my brokenness.

It happened to be my birthday. We were waiting until the weekend to celebrate, but I was so content sitting in a space where I could be my full self. In this, I wanted nothing but the company of Pops, as I affectionately called him.

Pops tapped me on my shoulder to tell me that my birthday dinner was done. Tonight, the menu was fried chicken and jambalaya with sausage, chicken, and shrimp—one of my favorites. I smiled thinking to myself, "This is what a good home should feel like."

Savoring each bite of food, Pops took me out of my thoughts abruptly and expressed that he had something he wanted to talk about. Fear overtook me as my mind rushed back to sleeping out in the cold or at houses with random men. I understood he was a full-time college student and community health worker, but I really had nowhere to go. Homeless was a place I didn't want to go back to—and definitely not on my birthday.

I sat up in the chair, "Yes, Pops. What is it?" I stayed calm; I could handle this. My being here was a luxury he didn't have to take on.

"Son, so I've been wanting to have this conversation for a while," he said. I was so nervous I couldn't eat; I found myself thinking of where I could go next. He continued slowly as it seemed millennia were in the space of his words, "I've been living with HIV for almost 10 years."

It was nothing that I thought I'd hear, but I still didn't know how to feel. I had never—to my knowledge—met someone who was living with HIV. So many myths scrambled through my mind, "Was he dying soon? Can I eat after him? Have I gotten it from using his restroom?" The fear I had of being put out was replaced with ignorant thoughts of this being a place unsafe for me.

As if he could hear my thoughts, he let me know that there was no need to worry and explained to me the routes of transmission of HIV. He expressed that he had acquired HIV when he was 18 years old from an older guy taking advantage of him who was now deceased. Though he saw many people pass away, no one ever sat with him to have a conversation on sex as a gay man.

That weekend, as a mini-birthday celebration, we went to a Many Men, Many Voices group where I learned more about living with HIV and how people acquire it. The secret I was holding inside is that I had never been tested. Now, knowing someone living with HIV, it made the possibility of me having a reactive result even more real.

That day, with his help, I took my first HIV test. I began sweating profusely. It seemed like every person I had any intimate connection with ran through my mind; the number of people I had written down on the intake form began to multiply in my head.

I'll never forget what he said before giving me my result, "Son, this fear is normal, but you can do something to reduce this fear. Now, HIV is not a death sentence, but if you don't want it, you have a choice. If this comes out negative, be more responsible with your sex."

I responded, "I'm never having sex again if it comes back negative."

He laughed, "I'll give you two weeks. Sex is natural, but it comes with responsibility."

Moments passed by with my heart racing until I finally got the result from my HIV test—negative. The fear I had in my mind was replaced by the responsibility of my body Pops spoke about. That day, I realized the best gift anyone could give me was the knowledge of my status.

Pops, who has now been living with HIV for 22 years, has always been the best at gift giving; first his heart, then his home, then the food, then my status. As a young person, it was the single most heroic feat of my life—having someone choose me and, through his lived experience, help to give me in celebration of my birthday what wasn't given to him—a choice.

IAN L. HADDOCK is the producer of *Outcry the Docu-Series* streaming exclusively on Prime Video. He serves as leader of The Normal Anomaly Initiative and president of Impulse Group Houston. Haddock is also the CDC's Let's Stop HIV Ambassador for Houston, Texas. Follow him on all social media at Ian L. Haddock.

PHOTO COURTESY OF IAN L. HADDOCK