



Fair Pricing Coalition Welcomes U.S. Launches of Mylan’s Tenofovir and Lamivudine Coformulation (Cimduo) and Efavirenz-based Single Tablet Regimens

Rollout of off-patent, off-exclusivity brand and generic antiretrovirals ushers in new era of cost as an important consideration in HIV treatment choice and coverage

Full Statement

Contact: Tim Horn

tim.horn@treatmentactiongroup.org

March 26, 2018 – The Fair Pricing Coalition (FPC), an ad hoc coalition of HIV and hepatitis C virus (HCV) activists, welcomes the U.S. Food and Drug Administration approvals and launches for Mylan’s Cimduo and Symfi Lo, with benchmark prices 40 percent lower than those of comparator drugs. Cimduo and two efavirenz-based products join a number of off-patent antiretrovirals (ARVs) – both generic and brands – entering the U.S. market that can potentially increase competition and lead to lower prices for purchasers and payors.

Cimduo, a coformulation of off-patent tenofovir disoproxil and lamivudine, is poised to compete with Gilead’s Truvada (tenofovir disoproxil/emtricitabine) and Descovy (tenofovir alafenamide/emtricitabine) for the treatment of HIV infection. Cimduo is not approved by the FDA for use as pre-exposure prophylaxis (PrEP to prevent HIV infection). The other combinations – coformulations of tenofovir disoproxil and lamivudine with either 400 mg efavirenz (Symfi Lo) or 600 mg efavirenz (Symfi) – are comparable with Gilead’s Atripla (tenofovir disoproxil/emtricitabine/efavirenz).

The Cimduo WAC (wholesale acquisition cost) price is estimated to be \$12,000 a year, compared with approximately \$20,100 for Truvada and Descovy. It is expected to be available in pharmacies in April. The WAC price for Symfi Lo, now available, is approximately \$19,600, compared to approximately \$32,700 a year for Atripla (Symfi, containing 600 mg efavirenz, has not yet launched). Actual prices will vary following required and negotiated discounts and rebates for public and private payors.

“This is a notable advancement in fair HIV drug pricing,” said Tim Horn, Chair of the FPC and Deputy Executive Director of HIV and HCV Programs of the Treatment Action Group. “Not only is Cimduo a safe and effective first-line regimen component for many people and the efavirenz-based single-tablet regimens good switch options for individuals doing well on Atripla, they may cut costs for individual patients and at least some public and private insurers. With the growing number of branded and generic drugs containing commonly used off-patent ARVs entering the U.S. market, differences in cost between comparable HIV treatment regimens are an important consideration. And while the societal benefits of reduced health care spending are well known, lower

treatment costs could translate to significantly increased access to HIV treatment and less discrimination within the health insurance market.”

The FPC engages with HIV drug manufacturers to advocate for low WAC pricing, along with significant discounts for public payors, not only to ensure that all people living with and vulnerable to HIV infection have access to essential treatment and prevention, but also in recognition of the larger societal benefits of affordable prescription drug pricing. In 2016 alone, the U.S. spent more than \$328 billion on retail prescription drugs, according to the Centers for Medicare & Medicaid Services.¹ HIV drug regimens, with annual WAC prices exceeding \$30,000, were the costliest Medicaid and third-costliest Affordable Care Act Exchange plan therapy class expenditures in 2017, according to per-member-per-year analyses conducted by Express Script.²

“HIV drug spending simply isn’t sustainable,” said Lynda Dee, a founding co-chair of the FPC and the Executive Director of AIDS Action Baltimore. “Less than half of the 1.1 million people living with HIV are on treatment and have suppressed viral loads. We need to get more people on treatment with the appropriate support systems to ensure linkage to, and engagement in, care and adherence. Resources are finite, however, especially for diseases of public health significance. We’re already seeing public and private insurers implementing significant cost-containment measures against high-cost regimens because they are priced beyond what taxpayers and the insurance markets can reasonably bear.”

Cost Savings

Generic drug products save the U.S. healthcare system billions of dollars a year: \$253 billion in savings were generated in 2016 alone, with \$1.67 trillion in savings over the past decade.³ This translates into public health care savings, private health insurance premium cost containment, and reduced out-of-pocket spending by consumers. With increasing demand for safe and effective off-patent drug products, competition between manufacturers results in further price reductions and increased savings.

Cimduo, Symfi, and Symfi Lo are not technically generic drug products, but instead brand-name products without exclusivity protections.⁴ This is the first time the U.S. Food and Drug Administration (FDA) has approved coformulations containing these specific ARVs – all of whose long-time patient protections have expired – so they are technically innovator products. Because Mylan did not conduct its own safety or efficacy research for Cimduo, Symfi, or Symfi Lo, they do not qualify for market exclusivity. In turn, other

¹ Centers for Medicare & Medicaid Services. National health expenditures 2016 highlights. Available from: <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/highlights.pdf>

² Express Scripts. 2016 drug trend report. <http://lab.express-scripts.com/lab/~/-/media/29f13dee4e7842d6881b7e034fc0916a.ashx>

³ Association for Accessible Medicines. Generic drug access and savings in the U.S. 2017. Available from: <https://accessiblemeds.org/sites/default/files/2017-07/2017-AAM-Access-Savings-Report-2017-web2.pdf>

⁴ Cimduo and Symfi Lo are technically “innovator multiple source drugs.” See: 42 CFR 447.502

manufacturers can commercialize similar products. The FPC encourages this, not only to increase the potential for additional cost savings but also to decrease the likelihood of egregious annual price increases.

Manufacturer competition has been critical to cost-containment for global HIV treatment programs, with annual negotiated prices of \$46–\$84 and ~\$97–\$160 for coformulations comparable to Cimduo and Symfi/Symfi Lo, respectively, available to many low-income national governments.⁵ “Mylan made minimal research and development investments in commercializing these drug products,” said Horn. “Forty percent lower WAC prices than comparator products are certainly a step in the right direction. But we can do much better in the U.S. with competition.”

Currently approved bona fide generic antiretrovirals available in the U.S. include stand-alone abacavir, atazanavir, efavirenz, lamivudine, nevirapine, ritonavir, tenofovir disoproxil, zidovudine, and coformulated abacavir/lamivudine, all of which are bioequivalent versions of FDA-approved innovator products.⁶

Cimduo and the efavirenz-based single-tablet regimen WAC prices have the potential to result in significant cost savings for some payors. Employer-based and Affordable Care Act Marketplace health insurance plans are well poised to pay significantly less for these products than they do for Truvada, Descovy and Atripla.⁷ Should commercial plans start placing cheaper medications like Cimduo, the Symfi products, or generics on their preferred drug lists, manufacturers of traditional brand-name ARVs and coformulations may start offering discounted pricing, likely in the form of increased rebates to pharmacy benefit managers (PBMs).⁸ The opposite is also true: manufacturers of traditional brand-name ARVs may increase prices, particularly if lower-cost products are cutting into utilization and sales.

“Lower-price brand and generic drugs are important market forces,” says Horn. “Fair pricing advocates can – and should – use this as leverage to ensure the lowest possible prescription drug costs for purchasers and payors. Any significant price increases of traditional brand-name drugs spurred by lower-cost competitors will be met with resistance.”

“Cost savings to commercial plans need to start translating into cost savings for patients and employers,” said FPC member David Evans of Project Inform. “Launching new drug products – including off-patent products – at low, transparent prices, with strict control over annual price increases, would negate the need for secretive deals between

⁵ Medecins Sans Frontiers. Untangling the Web of Antiretroviral Price Reductions. 18th Edition. 2016 July. https://www.msfnaccess.org/sites/default/files/HIV_report_Untangling-the-web-18thed_ENG_2016.pdf

⁶ Technically “generic multiple source drugs.” See: 42 CFR 447.502

⁷ Truvada, Descovy, and Atripla are technically “innovator single-source drugs.” See: 42 CFR 447.502.

⁸ Congressional Budget Office. How competition from generic drugs affects prices and quantities of prescription drugs. In: Effects of Using Generic Drugs on Medicare’s Prescription Drug Spending. 2010 September. <https://www.cbo.gov/publication/21800>

pharmaceutical companies, commercial plans, and their pharmacy benefit managers. Too many plans don't pass along cost savings in the form of reduced premiums, taxpayer savings, or lower out-of-pocket costs."

Because of the broken U.S. health care system, which has resulted in remarkably complex drug pricing regulations, it is less certain how much the introduction of Cimduo and the Symfi products will actually save Medicaid, AIDS Drug Assistance Programs (ADAPs), and 340B programs. Ceiling prices, from which discounts to these public payers are calculated, are confidential, determined by opaque processes involving discounts and rebates required by law or negotiated privately between manufacturers, purchasers, or public payors.

For example, Truvada is not only subject to a 23.1% price decrease off the confidential average manufacturer price (AMP; which on average is slightly lower than the WAC) for Medicaid, ADAPs, and 340Bs, the product's multiple price increases since its approval in 2004 have far exceeded inflation rates and have therefore triggered significant additional "penalty" rebates/discounts for these programs. Mylan will need to supplement its 40% list price differences (vs. Truvada, Descovy, and Atripla) and mandatory 23.1% rebate with substantial voluntary rebates to Medicaid, ADAPs, and 340B programs if they are to match or exceed the discounted Truvada, Descovy, and Atripla prices and result in significant cost savings.

"We strongly encourage Mylan and other multi-source ARV manufacturers to compete with each other and brand-name monopoly products across all payor systems, and to negotiate with groups like the ADAP Crisis Task Force," said FPC member Murray Penner, Executive Director of NASTAD. "It is fortunate that Medicaid, ADAPs, and 340B programs are able to take advantage of discounts and rebates for older ARVs, but given rapid changes in health care dynamics, including drugs preferred by clinicians or recognized by independent bodies and insurance marketplaces, good faith negotiations will be critical."

"These are very cheap drug products to manufacture and distribute – at profit – to meet global HIV treatment needs," said Horn. "Even after allowing for FDA fees and shipment costs, there's no reason why multi-source brand and generic products can't be discounted so that cost savings are ensured across all U.S. payor systems."

Some bona fide generic antiretrovirals may also be more expensive to some public payors, compared with post-rebate costs for older brand-name products. With competition among generic manufacturers, however, the potential for cost savings increases.

It should be noted that unlike true generics, pharmacies cannot automatically substitute Cimduo and Symfi products for their competitor combination products from Gilead Sciences. A clinician would have to specify the new combination on the prescription.

Pharmacies can, however, substitute brand-name products with generic competitors. These include Epzicom (abacavir/lamivudine), Reyataz (atazanavir), and Norvir (ritonavir).

Cost Implications for People Living with HIV

Lower out-of-pocket expenses associated with cheaper treatment regimen components and coformulations placed on less-expensive formulary tiers by commercial plans are a significant driver of generic drug product demand in the United States. However, all manufacturers with monopoly HIV drug products offer generous copay/coinsurance assistance, with ADAPs also providing out-of-pocket assistance. “If commercial plans actually place cheaper off-patent HIV drugs on tiers with lower cost-sharing – and there’s no guarantee they will – this could spell relief for people living with HIV covered by plans that don’t recognize manufacturer copay assistance programs – a practice that is growing,” said FPC member Andrea Weddle, Executive Director of the HIV Medicine Association (HIVMA).

Copay and coinsurance assistance provided by manufacturers may also be an important consideration for people living with HIV. Mylan, for example, is providing copay assistance for Symfi Lo (<https://www.activatethecard.com/symfi-lo/>) and is expected to offer copay assistance for Cimduo and Symfi as well. This may be subject to change if other manufacturers receive FDA approval for direct competitors. While generic manufacturers generally do not offer copay assistance – West-Ward, a manufacturer of generic ritonavir, is providing copay assistance through September 2018 – the FPC continues to advocate for these programs to defray out-of-pocket costs associated with HIV treatment.

Treatment Choice Implications for People Living with HIV

Cimduo and the generic coformulation of abacavir/lamivudine are expected to be the most acceptable to people living with HIV and providers because they are components of recommended initial regimens for most people living with HIV, according to the Health and Human Services’ *Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV*.⁹ Cimduo and abacavir/lamivudine, for example, are recommended for use in combination with the innovator product dolutegravir (Tivicay).

The Symfi products may have less appeal to people living with HIV starting treatment for the first time, as efavirenz plus tenofovir disoproxil and either emtricitabine or lamivudine are *Guidelines* recommended regimens only in certain clinical situations, largely due to the central nervous system side effects associated with efavirenz. However, tens of thousands of U.S. residents living with HIV are still using Atripla and,

⁹ HHS Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. 2017 Oct 17. <https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/37/>

for them, the reduced cost of the Symfi products – and the lower dose of efavirenz in Symfi Lo, which may be associated with fewer adverse events¹⁰ – may provide alternatives to consider.

Other generic drug-based products of interest for people with HIV include the protease inhibitor atazanavir and ritonavir for boosting which, like efavirenz, are recommended by the *Guidelines* in certain clinical situations.

Lamivudine is widely considered interchangeable with emtricitabine.¹¹ The interchangeability of tenofovir disoproxil with tenofovir alafenamide (a component of Descovy, Genvoya, Odefsey, and Biktarvy) is more controversial. As noted by the *Guidelines*:

TDF has been associated with lower lipid levels than TAF and ABC. However, TDF use has been associated with declines in kidney function, proximal renal tubulopathy (leading to proteinuria and phosphate wasting), and reductions in bone mineral density (BMD). These tenofovir toxicities are less common with TAF, which results in lower plasma tenofovir concentrations than TDF. As a result, the main advantages of TAF over TDF are TAF's more favorable effects on renal markers and BMD."

What remains unclear is if tenofovir alafenamide is a necessary regimen component option, compared with tenofovir disoproxil, for all people living with HIV, notably those beginning HIV treatment with normal kidney function and bone health. For such patients, tenofovir disoproxil-inclusive regimens like Cimduo may be a suitable option, in alignment with the *Guidelines*.¹²

Another implication is payor preferences for lower-cost drug products that may necessitate breaking up single-tablet regimens. While single-tablet regimens, particularly those recommended by the *Guidelines* for most people living with HIV, are preferred by some patients and providers because they are easier to use and are associated with fewer monthly copayments, clinical trial data to support or refute the superiority of single-tablet regimens over once-daily multi-tablet regimens—which would include regimens containing Cimduo and generic abacavir/lamivudine—are limited.¹³

¹⁰ Efficacy and safety of efavirenz 400 mg daily versus 600 mg daily: 96-week data from the randomised, double-blind, placebo-controlled, non-inferiority ENCORE1 study. *Lancet Infect Dis*. 2015 Jul;15(7):793-802. doi: 10.1016/S1473-3099(15)70060-5.

¹¹ Ford N, Hill A, Vitoria M, Mills EJ. Editorial commentary: Comparative efficacy of lamivudine and emtricitabine: comparing the results of randomized trials and cohorts. *Clin Infect Dis*. 2015 Jan 1;60(1):154-6. doi: 10.1093/cid/ciu767.

¹² HHS Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. 2017 Oct 17. <https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/37/>

¹³ HHS Panel on Antiretroviral Guidelines for Adults and Adolescents. Limitations to treatment safety and efficacy: Adherence to the continuum of care. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. 2017 Oct 17. <https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/30/adherence>

“Once-daily multi-tablet regimens containing Cimduo or abacavir/lamivudine would undoubtedly be safe, effective, and easy to take by many people living with HIV,” said Horn. “FPC strongly encourages people living with HIV to discuss their treatment choices in the context of drug pricing and cost savings with their providers. We all share the burden of high health care costs and drug prices, some more directly than others. Even in the absence of personal benefits of starting or switching to a lower-cost regimen consistent with today’s standard of care, there are societal benefits to consider.”

“Payor preferences for cheaper competitive products, in the form of step therapy requirements and denials of coverage for higher-cost monopoly products, can be intrusive and dangerous. People living with HIV are not a homogenous patient population; individualized therapy to meet adherence needs is still essential,” said Horn. “To prevent these cost-containment measures, we urge the leading traditional manufacturers of HIV drug products—Gilead, ViiV, Merck, and Janssen—to price their products competitively with emerging lower-price options.”

Community advocates, health care providers, and people living with HIV should watch for overly restrictive insurance company practices, including cumbersome processes associated with switching from either tenofovir disoproxil- to tenofovir alafenamide-containing regimens or multi-tablet to single-tablet regimens. FPC encourages the reporting of egregious examples via the SpeakUP portal maintained by the AIDS Foundation of Chicago and the Center for Health Law and Policy Innovation at Harvard Law School: [SpeakUP.HIV](https://www.speakup.hiv).

###