

HIV PLAYBOOK

September 2023

Supply Chain Incentives: Truvada and Descovy

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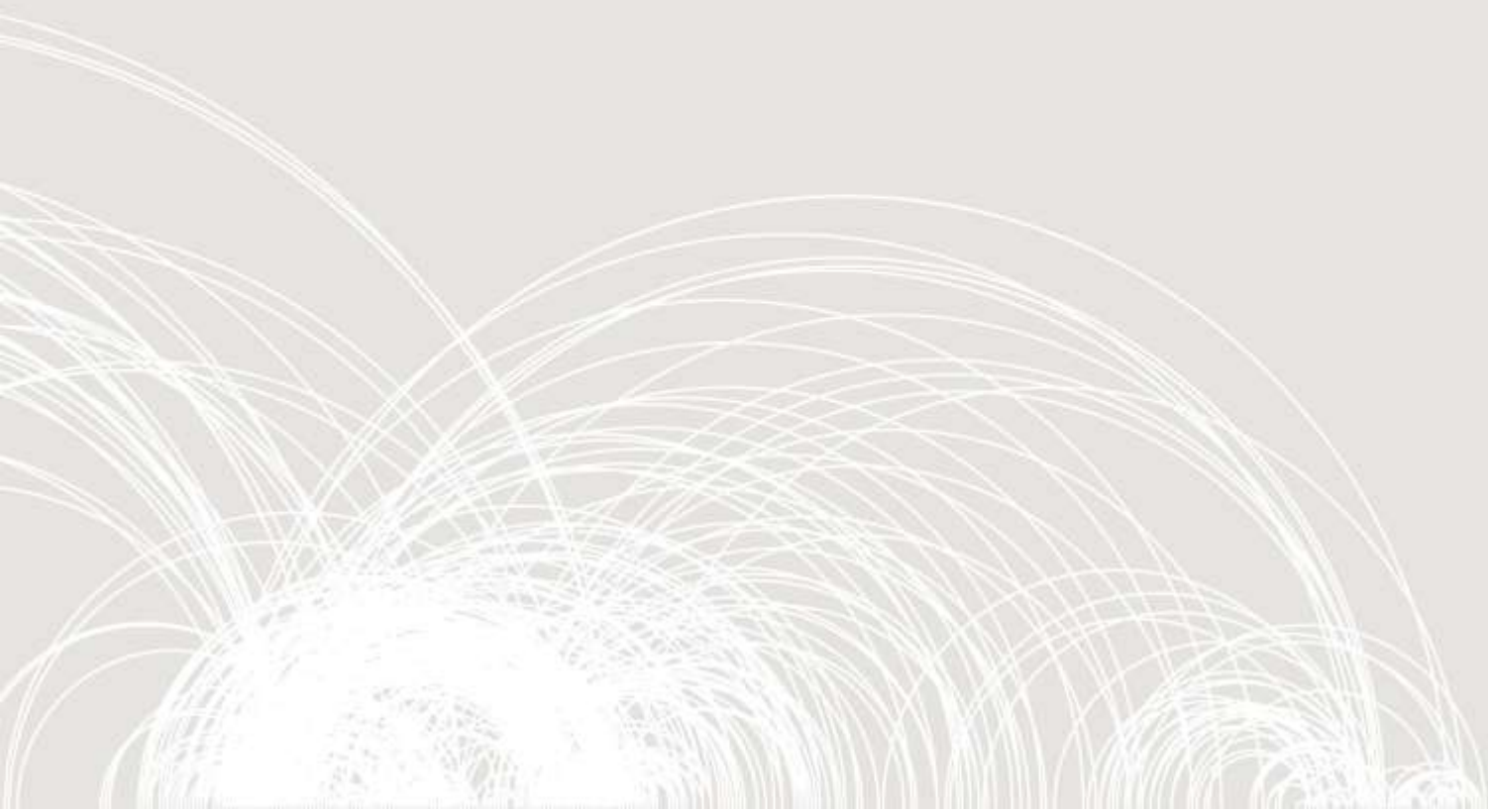


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About This Series

This paper is organized to highlight each medication or therapy in this series in three phases: production, commercialization, and access.

Within production, there are critical steps and decisions that manufacturers make regarding research and development, patenting, and manufacturing.

From there, commercialization is intended to look closely at how a product is marketed, labeled, and regulated, and the resultant impact of those decisions on the price of each featured product.

The final step in the process is access, how product acquisition (moving from manufacturer, through wholesalers, and on to pharmacies) and distribution (PBMs, payers, and providers) shapes patient access, which is so often impacted by cost.

Introduction

Approximately 1.2 million people in the United States are living with Human Immunodeficiency Virus (HIV) infection. While there were over 30,000 new HIV infections reported in 2020, the estimated number of new HIV infections has continued to drop each year since 2016 and annual infections have fallen by two-thirds since the height of the epidemic in the 1980s.¹

The overall decline in new infection rates over the last decade can be attributed to various infection prevention strategies, including investments in education and awareness, greater access to testing, as well as the increased use of pre-exposure prophylaxis (PrEP).² PrEP is recommended for all individuals who have an increased risk of contracting HIV. The primary factors that make an individual at increased risk for contracting HIV are those who engage in high-risk sexual behavior, such as having sex with a partner who has an unknown or detectable HIV viral load or consistent unprotected sex, as well as people who inject drugs or share needles with people who have HIV.³ When taken daily, PrEP reduces the risk of contracting HIV through sex by 99% and through intravenous drug use by 74%.⁴

Today, there are two small-molecule brand name PrEP medications, Truvada (Emtricitabine/tenofovir disoproxil fumarate; TDF) and Descovy (Emtricitabine/tenofovir alafenamide fumarate; TAF). Both are manufactured by Gilead Sciences, Inc. ("Gilead") and are antiretroviral drugs taken in pill-form daily by people who do not have HIV but are at high risk of contracting the disease. The drugs differ in the type of fumarate used in the medication (i.e., disoproxil vs. alafenamide), but are otherwise similar in their efficacy and safety profiles. PrEP is only available by prescription and a patient must first be seen by a licensed health care provider and test negative for HIV before starting the medication. Patients will also likely need to see their health care provider every three months and continually test negative for HIV to stay on the medication.

Truvada, initially approved as a treatment for people diagnosed with HIV, was approved as the first PrEP medication in 2012.⁵ Seven years later, in 2019 Gilead launched their second PrEP medication,

¹ Centers for Disease Control and Prevention. (2022, September 2). *HIV Incidence*. Retrieved March 21, 2023, from <https://www.cdc.gov/hiv/statistics/overview/in-us/incidence.html>

² Smith, D. K., Sullivan, P. F., Cadwell, B. L., Waller, L. A., Siddiqi, A. E. A., Mera-Giler, R., Hu, X., Hoover, K. W., Harris, N., & McCallister, S. (2020). Evidence of an Association of Increases in Pre-exposure Prophylaxis Coverage With Decreases in Human Immunodeficiency Virus Diagnosis Rates in the United States, 2012–2016. *Clinical Infectious Diseases*, 71(12), 3144–3151. <https://doi.org/10.1093/cid/ciz1229>

³ Centers for Disease Control and Prevention. (2022a, July 6). *Deciding to Take PrEP*. Retrieved March 21, 2023, from <https://www.cdc.gov/hiv/basics/prep/prep-decision.html>

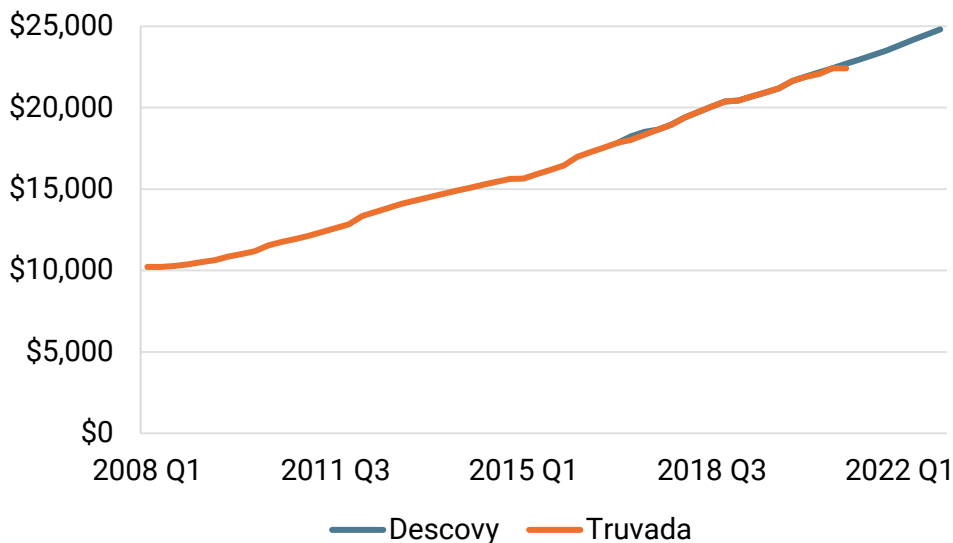
⁴ Centers for Disease Control and Prevention. (2022a, June 6). *PrEP Effectiveness*. Retrieved March 21, 2023, from <https://www.cdc.gov/hiv/basics/prep/prep-effectiveness.html>

⁵ US Food & Drug Administration. (2006, January 31). *Drug Approval Package: Truvada (Emtricitabine and Tenofovir Disoproxil Fumarate)*. Retrieved March 21, 2023, from https://www.accessdata.fda.gov/drugsatfda_docs/nda/2004/021752s000_TruvadaTOC.cfm

Descovy⁶—one year before Truvada’s initial patent expired in 2020. Today there are a dozen generic PrEP medications available.⁷ However, adoption of generic alternatives has been slow due to layered incentives within the PrEP supply chain, and important regulatory and market considerations.

Despite PrEP’s high efficacy rates, it is estimated that nearly three quarters (73%) of individuals who could benefit from PrEP have not been prescribed the medication.⁸ Further, the rate at which patients have switched from brand name drugs to less expensive generic alternatives has been very low, despite the high costs for a yearly course of branded products like Truvada (\$22,415) and Descovy (\$24,807).⁹ While the overall low adoption rate of PrEP could be due to a number of factors such as trust in the health care system, stigma, and access; this playbook explores why existing policy decisions and business models incentivize key actors to promote higher-priced, brand name drugs.

Exhibit 1. WAC Cost per Year or Course



Source: SSR Health

Note: Cost per year or course of therapy is estimated by multiplying estimated price per unit at the product level by the maximum annual or course dosage included on the product’s package insert assuming a US patient of representative weight or body surface area, as determined using National Center for Health Statistics Data.

⁶ US Food & Drug Administration. (2019, October 3). *FDA approves second drug to prevent HIV infection as part of ongoing efforts to end the HIV epidemic* [Press release]. <https://www.fda.gov/news-events/press-announcements/fda-approves-second-drug-prevent-hiv-infection-part-ongoing-efforts-end-hiv-epidemic>

⁷ *Generic Truvada Availability*. (2023, March 9). Drugs.com. Retrieved March 21, 2023, from <https://www.drugs.com/availability/generic-truvada.html#Has%20A%20Generic%20Version%20of%20Truvada%20Been%20approved?>

⁸ AHEAD. (2022, March). *The Six EHE Indicators: National Data*. Retrieved March 21, 2023, from <https://ahead.hiv.gov/data/prep-coverage>

⁹ Data from SSR Health.

Impact of Incentives

Production

Research and Development

Gilead's research and development of drugs to treat or prevent HIV began decades ago. At any given time in development, Gilead had multiple HIV drug candidates that could be classified as either TDF or TAF. For the purposes of this section we will refer to Truvada (TDF) and Descovy (TAF).

From 2002 to 2003, Gilead conducted a clinical trial comparing Truvada and Descovy in a head-to-head evaluation of efficacy, safety, and tolerability, and in a Q4 2003 shareholder report announced the continued clinical development of Descovy "based on favorable Phase I/II results" of the trial.¹⁰ In 2004, Truvada was approved by the Food and Drug Administration (FDA) for HIV treatment (but not yet for PrEP) and in the same year, Gilead surprisingly announced that it was stopping its research on Descovy and delaying the publication of clinical trial data.¹¹

In 2010, Gilead announced that it was restarting its research into Descovy, and in 2012, Truvada was approved for PrEP by the FDA.¹² In 2016, Descovy was approved to treat HIV, and by 2019 it was approved for PrEP.¹³ The deliberate pause, and subsequent resumption, of efforts to develop Descovy eventually positioned Gilead to bring Descovy to market just ahead of when they expected generic competitors of Truvada to come to market.

In 2019, Gilead launched Descovy at \$20,437, allowing Gilead to transition patients on Truvada to Descovy ahead of the first Truvada generic launch in 2020.¹⁴ The practice, when a manufacturer selectively introduces a new drug that features minor product reformulations in an effort to thwart generic competition, is often referred to as "product hopping" and is not uncommon.¹⁵ It also has profound implications for what consumers pay to access their medications. One analysis estimates that the cost of product hopping for just five brand name drugs cost the U.S. health care system almost \$5 billion annually.¹⁶ In the case of PrEP, this strategy of product hopping materialized in patients being

¹⁰ Dickson, S., & Killelea, A. (2021). Intentionally Delayed Pharmaceutical Innovation Under Perverse Incentives: Gilead's HIV Pipeline As A Case Study. *Health Affairs Forefront*. <https://doi.org/10.1377/forefront.20210614.619677>

¹¹ Ibid.

¹² Ibid.

¹³ Ibid.

¹⁴ Data from SSR Health.

¹⁵ FTC Files Amicus Brief Explaining that Pharmaceutical "Product Hopping" Can Violate the Antitrust Laws. (2015, October 1). Federal Trade Commission. <https://www.ftc.gov/news-events/news/press-releases/2015/10/ftc-files-amicus-brief-explaining-pharmaceutical-product-hopping-can-violate-antitrust-laws>

¹⁶ Brill, A. (2020). The Cost of Brand Drug Product Hopping. Matrix Global Advisors. Retrieved June 7, 2023, from <https://www.affordableprescriptiondrugs.org/app/uploads/2020/09/CostofProductHoppingSept2020-1.pdf>

proactively transitioned from Truvada to Descovy prior to generic launch, rendering the Truvada generics (that is, generic TDF) as a less comparable substitute to Descovy (that is, patented TAF) and ultimately, diminishing their uptake.

Commercialization and Access

Marketing

As Gilead prepared for the launch of Descovy, they engaged in marketing to both providers and consumers, focusing on the benefits of Descovy over Truvada treatments. This enabled Gilead to capture patients who would have switched to the Truvada generic the following year. Their marketing was successful. Gilead transitioned 49% of Truvada utilization over to Descovy, according to Part D data, even though the switch from Truvada to Descovy was found to be unwarranted in five of six switches, on average.^{17,18} According to Kenyon Farrow, the managing director of Advocacy and Organizing of the group PrEP4All, “What seems to be happening is that doctors are being encouraged to switch patients to Descovy based on the surface impression that it has a better safety profile, but for most of us, generic Truvada is perfectly safe. The switch to Descovy has more to do with Gilead trying to hold onto its market share of PrEP users in the face of the generics.”¹⁹

Acquisition

The 340B program is a federal drug pricing program that allows qualified clinics and hospitals to buy outpatient drugs at steep discounts so that those qualified clinics and hospitals can capture the difference between their drug acquisition cost and the reimbursement they receive from payers, often referred to as “spread” pricing. Under the intent of the law, these entities then use spread pricing to offset the costs of treating low-income or uninsured individuals. The program enables safety-net hospitals, clinics, and other entities that serve vulnerable populations the ability to stretch resources and care for more patients than they otherwise would be able to without the program.²⁰ A consequence of this incentive system, however, is that these entities can achieve greater impact by prioritizing acquisition of medications that have a higher spread price, which often translates to higher-priced drugs against which greater discounts can be captured.

¹⁷ Dickson, S., & Killelea, A. (2021). Intentionally Delayed Pharmaceutical Innovation Under Perverse Incentives: Gilead’s HIV Pipeline As A Case Study. *Health Affairs Forefront*. <https://doi.org/10.1377/forefront.20210614.619677>

¹⁸ Murphy, T. (2021, October 7). Are Health Centers Needlessly Prescribing Pricey Descovy for PrEP Because They Get a Government Kickback? *The Body: The HIV/AIDS Resource*. Retrieved March 21, 2023, from <https://www.thebody.com/article/needlessly-prescribing-pricey-descovy-for-prep>

¹⁹ Murphy, T. (2021, October 7). Are Health Centers Needlessly Prescribing Pricey Descovy for PrEP Because They Get a Government Kickback? *The Body: The HIV/AIDS Resource*. Retrieved March 21, 2023, from <https://www.thebody.com/article/needlessly-prescribing-pricey-descovy-for-prep>

²⁰ Clark, B., & Puthiyath, M. S. (2022). The Federal 340B Drug Pricing Program: What It Is, and Why It’s Facing Legal Challenges. *The Commonwealth Fund*. <https://doi.org/10.26099/c4z8-pf65>

In the case of PrEP, the 340B program allows covered entities to obtain PrEP at steeply discounted prices, however they are reimbursed per the terms of the payer for that patient, whether it is Medicare, Medicaid, or commercial insurance. Because there is a greater spread from prescribing more expensive drugs, such as Truvada and Descovy, compared to inexpensive generic alternatives, Truvada and Descovy are shielded from more typical competitive pricing market dynamics that play out when generic drugs enter the U.S. market. In many settings which see a large share of at-risk individuals, including Federally Qualified Community Health Centers and clinics enrolled in the Ryan White program, this reliance on spread pricing is done with the goal to increase access to needed care for the vulnerable patient population. Ultimately, however, this heavy reliance on spread pricing contributes to the observed pricing dynamics.²¹

Distribution

An important element in patient access to prescribed medications is their insurance coverage. PrEP is covered under Medicare Part D, but patient cost-sharing can be high and is estimated to be approximately \$3,500 annually for a patient with traditional Medicare and no low-income subsidies.²² State Medicaid programs must cover at least one PrEP medication and are further incentivized to provide it at no cost to enrollees in return for a one percent increase in the federal match rate for providing the medication and any medically necessary testing services associated with taking it.²³

In 2020, TDF was given an “A” recommendation by the U.S. Preventive Services Task Force (USPSTF).²⁴ Under the Patient Protection and Affordable Care Act, evidence-based items or services that have an “A” or “B” rating must be covered without cost-sharing. In effect, this means that at least one TDF PrEP option (e.g., Truvada or generic) must be available at no cost to enrollees in most private health insurance plans.²⁵ Prior to this recommendation, the high list price for PrEP meant that patients often needed to seek prior authorization or use special mail-order pharmacies to get their medication.²⁶ While this is an improvement for those on Truvada, it is not the case for those patients currently taking

²¹ Ballreich, J., Levensgood, T. W., & Conti, R. M. (2022). Opportunities and Challenges of Generic Pre-Exposure Prophylaxis Drugs for HIV. *Journal of Law Medicine & Ethics*, 50(S1), 32–39. <https://doi.org/10.1017/jme.2022.33>

²² Tseng, C., Dudley, R. A., Chen, R., & Walensky, R. P. (2020). Medicare Part D and Cost-Sharing for Antiretroviral Therapy and Preexposure Prophylaxis. *JAMA Network Open*, 3(4), e202739. <https://doi.org/10.1001/jamanetworkopen.2020.2739>

²³ Medicaid and People with HIV. (2023, March 27). KFF. <https://www.kff.org/hiv/aids/issue-brief/medicaid-and-people-with-hiv/>

²⁴ Prevention of Human Immunodeficiency Virus (HIV) Infection: Preexposure Prophylaxis. (2019). <https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/prevention-of-human-immunodeficiency-virus-hiv-infection-pre-exposure-prophylaxis>

²⁵ Coverage of Certain Preventive Services Under the Affordable Care Act. (2015, July 14). Federal Register. <https://www.federalregister.gov/documents/2015/07/14/2015-17076/coverage-of-certain-preventive-services-under-the-affordable-care-act>

²⁶ Farrow, K. (2022). The Downstream Impacts of High Drug Costs for PrEP Have Hindered the Promise of HIV Prevention. *Journal of Law Medicine & Ethics*, 50(S1), 47–50. <https://doi.org/10.1017/jme.2022.35>

Descovy, which as of August 2023 had not yet been officially included in the USPSTF recommendation and may still be subject to prior authorization and co-pays.

The U.S. Public Health Service Clinical Guidelines recommend patients subsequently see their health care provider every three months for testing to confirm they remain HIV negative to continue receiving the medication.²⁷ This high level of engagement with a provider may contribute to structural, logistical, and financial barriers to access PrEP for many patients. Co-pays for visits, lab tests, and prescription refills can create barriers for patients over time. Combined with the high price of PrEP itself, costs of continuing treatment may negatively impact medication adherence.

Patient Implications

Note: Patient scenarios are meant to be illustrative only. The goal of these scenarios is not to provide exact prices, but to demonstrate the patient experience while accessing medications and the ways price is impacted by upstream incentives. Prices are based on publicly available information when possible (and cited accordingly) and based on good faith estimates when prices were not available.

In the scenarios below, we follow a man who engages in high-risk behaviors for contracting HIV and is seeking a prescription for PrEP. He is enrolled in a high-deductible health plan through employer-sponsored insurance and has access to a few care settings in his local area such as a Ryan White clinic and an independent primary care practice, both of which provide HIV care. These scenarios will differ primarily on the financial structure and incentives of the care setting to treat the same medical condition with different drug therapies—Descovy versus Truvada. This difference will result in substantially different out-of-pocket drug costs for the patient.

Scenario 1

The patient seeks care from a Ryan White clinic which provides HIV and AIDS care in his local community. After a physician consultation and upon testing negative for HIV, the Ryan White clinic prescribes Descovy. Because the Ryan White clinic is a 340B qualified entity and Descovy is included in the clinic's 340B program, prescriptions for Descovy provide a financial benefit for the clinic due to its higher spread price. The WAC, or list price, for a year of Descovy as of Q4 2022 was approximately \$25,000. The patient will first pay his \$3,000 deductible (if not already met), and then will be responsible for a 20% patient coinsurance on the remaining cost of the drug. In sum, the patient's out-of-pocket for the year (deductible plus coinsurance) is \$7,400, which breaks down to a monthly average cost of \$617.

²⁷ US Public Health Service. (2021). Clinical Practice Guideline: Preexposure Prophylaxis for the Prevention of HIV Infection in the United States. <https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf>

Scenario 2

The patient seeks a prescription for PrEP from an independent primary care practice instead of the Ryan White clinic. The primary care practice is not a 340B qualified entity and does not have 340B incentives to prescribe drugs with a high price spread. After a physician consultation and upon testing negative for HIV, the primary care practice prescribes generic Truvada. Due to the Affordable Care Act and TDF's "A" recommendation by the USPSTF, the patient's insurance covers generic Truvada with no cost-sharing obligations. As a result, the patient's out-of-pocket costs for generic Truvada is \$0.

Scenario 1	Scenario 2
Descovy	Generic Truvada
Patient seeks care from a Ryan White Clinic, which participates in the 340B program.	Patients seeks care from an independent primary care practice (not a 340B qualified entity).
The 340B program creates an incentive to prescribe drugs with a higher price spread, so the patient is prescribed Descovy.	The primary care practice is not a 340B qualified entity and does not have an incentive to prescribe drugs with a higher price spread, so the patient is prescribed generic Truvada.
Assuming the patient has not met their annual deductible, patient is responsible for deductible of \$3,000 plus 20% coinsurance on the remaining cost.	Due to the Affordable Care Act and TDF's "A" recommendation by the USPSTF, the patient's insurance covers generic Truvada with no cost-sharing obligations.
The patient's out-of-pocket for the year is \$7,400, which breaks down to a monthly average cost of \$617.	The patient's out-of-pocket for the year is \$0.

Conclusion

PrEP is an effective tool in the prevention of the spread of HIV. However, strategies employed by some manufacturers of PrEP medications as well as the legal and market structures means that a large portion of those who are eligible for treatment experience higher prices and barriers to adherence.

Acknowledgements

This research was made possible with support from Arnold Ventures.

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