NASTAD

PrEP GENERICS ENTERING THE US. MARKET:

FREQUENTLY ASKED QUESTIONS (FAQS)

The HIV pre-exposure prophylaxis (PrEP) landscape is rapidly changing. With the introduction of new drugs approved for PrEP and generic options becoming available, many changes are underway or on the horizon. This FAQ provides current information on the introduction of PrEP generics, potential coverage changes related to the changing PrEP drug market, and the impact on PrEP access.

WHAT DRUGS ARE AVAILABLE FOR PrEP?

The US Food and Drug Administration (FDA) has approved two medications for PrEP:

- Tenofovir disoproxil fumarate and emtricitabine (TDF/FTC) was approved for PrEP by FDA in 2012. Brand name: Truvada® by Gilead Sciences. Generic TDF/FTC is now available from Teva Pharmaceuticals USA.
- Tenofovir alafenamide and emtricitabine (TAF/FTC) was approved for PrEP by FDA in October 2019. Brand name: Descovy® by Gilead Sciences. TAF/FTC was approved with limitations and is indicated only for gay, bisexual, and other men who have sex with men as well as transgender women.

On November 17, 2020 FDA designated long-acting, injectable cabotegravir for PrEP as a break-through therapy, expediting consideration for approval. A final FDA approval decision is expected by May 2021. Cabotegravir is manufactured by ViiV Healthcare.

WHEN WILL GENERIC TDF/FTC BECOME AVAILABLE IN THE US?

On October 2, 2020, Teva Pharmaceuticals USA began selling generic TDF/FTC in the US. The early availability of a single generic formulation of TDF/FTC stems from a lawsuit settlement five years earlier. Through that lawsuit, Gilead granted Teva exclusive rights to commercialize its version of TDF/FTC one year before key patents protecting Truvada's monopoly expire.

In addition to Teva, three other generic manufacturers have received FDA approval to market TDF/FTC as of October 21, 2020: Amneal Pharmaceuticals, Aurobindo Pharma, and Zydus Pharmaceuticals. Gilead and Teva's confidential settlement may mean only one generic product is available in the US for at least six months. Up-to-date information on generics approved for commercialization in the US is available on the FDA Orange Book. The four manufacturers listed above have an "AB" bioequivalence rating for their TDF/FTC

products. AB bioequivalence indicates that pharmacies can switch patients from the brand-name drug to the generic therapeutic equivalent.

Information on the safety and therapeutic equivalence of generic drugs, including information about the approval process and patient education resources, is available on the FDA website.

HOW MUCH DOES GENERIC TDF/FTC COST?

- As of October 14, 2020, the wholesale acquisition cost price per pill of Teva's generic TDF/FTC is $48.51, which is approximately 21 percent lower than the brand-name version. NASTAD does not anticipate that Teva's TDF/FTC's list price will go down during its exclusivity period. The most significant price decreases typically come about once multiple generic manufacturers compete in the same market. Once Teva's exclusivity period ends, NASTAD expects competition to be robust. However, until additional competitors join the market, the price difference between the generic and the brand name drugs might not be enough to drive coverage changes across most payers.

  Competition in the drug market helps manage costs to support sustainability, expansion, and affordability through our public and private payer systems. It will also ensure that public health programs, community programs, educational systems, prisons/jails, and people vulnerable to HIV who are underinsured or struggle with high cost-sharing have access to PrEP.

DOES COMPETITION DRIVE PRICES DOWN?

- The introduction of generic coformulations of abacavir and lamivudine (ABC/3TC), approved as a component of HIV treatment, is an excellent example of generic competition. In late 2016, the year a single generic competitor entered the market, pharmacy acquisition prices per bottle (30 tablets) were approximately $912 for the generic version and $1,230 for brand-name Epzicom. By June 2017, with multiple competitors, the average price of ABC/3TC was $206 a bottle. As of late November 2020, the average price for generic ABC/3TC is approximately $65/bottle, with about six competitors.

  Generic competition is primarily driven by demand and utilization. Since NASTAD expects significant demand for, and growing use of, generic TDF/FTC, we expect several manufacturers to enter the PrEP market and compete.

GENERIC DRUG BIOEQUIVALENCE

Generic drugs are comparable to the FDA-approved brand-name drug in dosage form, strength, route of administration, quality, performance characteristics, and intended use. These similarities help to demonstrate **bioequivalence**, meaning a generic medicine works in the same way and provides comparable safety and efficacy as its brand-name version. Generic drugs may have a different size, color, flavor, and inactive ingredients; however, the active pharmaceutical ingredient (API) must be the same.

Due to the FDA's exclusivity periods and various patents on brand-name medications, generics are often released after a set period of time. The exclusivity period and patents serve, in part, as incentives to manufacturers to bring a new drug to market. Once the FDA exclusivity period ends (generally 5 to 7 years after approval), generic manufacturers can file an abbreviated new drug application with the FDA for approval, though there may still be patents protecting the brand-name product. Lawsuits then typically ensue. Depending on the lawsuit's outcomes, or if the patent protections have run out, both FDA approval and commercialization can occur.

Manufacturers rigorously test generic medications in compliance with stringent FDA standards. These include ensuring the active ingredients, strength, administration method, and use indications, among other considerations, are the same as the brand-name version. Instead of expensive and time-consuming animal and human safety/efficacy studies, generic manufacturers must conduct bioequivalence studies, demonstrating that their product achieves comparable active pharmaceutical ingredient levels in the blood and/or tissue as the brand-name products.

WILL COPAY ASSISTANCE PROGRAMS BE AVAILABLE FOR GENERIC PrEP?

- Teva has made available a copay savings card/coupon for TDF/FTC providing up to $600 per month for six months. Gilead Sciences has not announced any changes to its Advancing Access Copay Relief for Truvada or Descovy program at this time. As the PrEP drug market changes, it is crucial to keep in mind that manufacturers of brand-name products may cease copay assistance for their products where there is generic competition. Similarly, where Teva currently offers copay assistance for its generic version of TDF/FTC, this program may cease when other versions of generic TDF/FTC enter the market.

  Starting in January 2021 (and earlier for some employer and student health plans), many private insurance plans are expected to provide $0 cost-sharing for at least one PrEP product, so many patients should not need copay assistance programs. This change is an example of the patient protections available through the Affordable Care Act (ACA). The US Preventive Services Task Force (USPSTF) gave PrEP an "A" recommendation, placing it on the list of preventive services that health plans must cover at no cost to the patient. This requirement also applies to Medicaid expansion benefits.

  With full implementation of the USPSTF recommendation, many of the affordability challenges will significantly improve for patients. However, there is still much work to be done to ensure that insurance regulators, state Medicaid programs, and issuers fully implement the USPSTF requirements. Additional work in this area includes guaranteeing access to Descovy without cost-sharing when clinically indicated and ensuring access to clinic visits and laboratory services recommended for PrEP without cost-sharing.

THE USPSTF "A" RECOMMENDATION FOR PrEP

In May 2019, USPSTF issued a grade A recommendation for TDF and TDF/FTC as PrEP. With this recommendation, ACA patient protections will require Medicaid expansion programs and commercial health plans to cover PrEP, without cost-sharing, starting with the 2021 plan year. Traditional Medicaid programs are not required to cover PrEP without cost-sharing but receive an increased federal match for covering USPSTF Grade A and B services without cost-sharing. The USPSTF recommendation means that most private insurance plans could eliminate patient out-of-pocket costs for PrEP, including deductibles, copayments, or coinsurance.

Recent federal guidance indicates that health plans should also cover the recommended clinical visit and laboratory services for PrEP without cost-sharing, and expanded Medicaid programs must also guarantee access to PrEP for beneficiaries at high risk for HIV.1 Existing sub-regulatory guidance on similar USPSTF recommended services have similarly required coverage of ancillary services that are inextricable from the underlying intervention.

NASTAD continues to advocate for the inclusion of all PrEP-related clinical services (e.g., U.S. Centers for Disease Control and Prevention-recommended labs and provider follow-up visits) in federal and state sub-regulatory guidance for commercial insurance plans, as well as with commercial insurance carriers. How health plans implement the USPSTF recommendation will directly impact the coverage and cost of care for PrEP patients.

WILL THE COVERAGE OF PrEP CHANGE BECAUSE OF THESE MARKET DYNAMICS?

- NASTAD anticipates the availability of generic equivalents will impact health plan coverage moving forward. As generics enter the TDF/FTC market, commercial insurers will have an additional incentive to prefer generic TDF/FTC to contain their costs.

  In addition to charging higher out-of-pocket costs, Medicaid programs and commercial insurers often use "utilization management tools," such as prior authorization, to control the use of high-cost medications. When a prior authorization requirement is in place, a prescriber must attest to a patient's need for a pharmacy or medical service before the health plan will cover it. These utilization management tools will still be available to health plans, even with the full implementation of the USPSTF recommendation.

At least one national health insurance carrier is now limiting the use of TAF/FTC to individuals with a clinical need for the drug through prior authorizations. United Healthcare sent letters to PrEP providers and members on PrEP indicating that effective on September 1, 2020, TAF/FTC for PrEP requires prior authorization based on medical necessity for coverage. The policy is intended to drive plan members to opt for the generic TDF/FTC equivalent. In this case, the health plan has interpreted the preventive service protection narrowly, claiming that they are only required to cover one drug for PrEP within the class and not every product available in the market. Although the insurance carrier is limiting access to the brand-name drug, it also agreed to cover the cost of clinical visits and lab tests with no cost-sharing while providing a pathway to access the TAF/FTC regimen whenever TDF/FTC is not indicated.

Utilization management policies are never desirable for patients or providers. However, if a health plan imposes utilization management tools on PrEP drugs, payers and regulators must ensure that these policies are clinically sound, adhere to federal guidelines, don't restrict access to clinically indicated regimens, and are not discriminatory or stigmatizing.

At the federal level, the Centers for Medicare and Medicaid Services (CMS) has started allowing health plans to exclude part of a manufacturer's copay assistance program from the member's contribution toward their out-of-pocket maximum if a generic equivalent is available and indicated. This rule affirms the use of copay accumulator policies when generic equivalents are available. The final rule is poised to begin implementation in 2021 unless further action is taken.

At present, the Medicaid ceiling price for Truvada is significantly lower than the ceiling price for Descovy and is expected to be considerably lower than the ceiling price for single-source generic TDF/FTC. This price difference could result in Medicaid programs opting to cover the brand-name drugs instead of the generic TDF/FTC version or the TAF/FTC until robust generic TDF/FTC competition ensues.

HOW WILL THESE CHANGES IMPACT 340B-COVERED ENTITIES?

- The cost savings that 340B-covered entities receive from dispensing Truvada can be substantial due to a mandatory discount of 23.1% off the average manufacturer price and mandatory discounts associated with price increases that exceed a standard rate of inflation since the FDA approved the product in 2004.[2] While 340B-covered entities may generate some savings on generic TDF/FTC, they will not be as significant as those for Truvada.

  340B-covered entities that prescribe PrEP have reported that the manufacturer offers significant voluntary discounts on Descovy to match the mandatory discounts that agencies receive on Truvada®. This voluntary discount could serve as an incentive for clinicians to prefer Descovy once generic TDF/FTC is available; however, the manufacturer provides this supplemental discount at its sole discretion.

  Restrictive formulary coverage of PrEP will profoundly impact 340B-covered entities. Once robust generic competition ensues, entities will likely be able to procure TDF/FTC at prices below those for 340B-discounted Truvada® or Descovy®, potentially improving affordability for uninsured and underinsured patients. However, if commercial insurers move to prefer generic TDF/FTC and restrict Descovy access to those with a clinical need for the drug (e.g., changes in renal or bone biomarkers while using TDF/FTC), 340B entities may be unable to secure program income on many of its insured patients.

  Agencies that depend on 340B program income to cover the cost of labs, clinical visits, outreach, and support services for their patients are therefore encouraged to diversify funding streams, expand health care services, broaden the range of medications subject to 340B discounting, and maximize billing opportunities for clinical and support services to avoid gaps in service and provider sustainability.

WHO CAN I REACH OUT TO WITH CONCERNS ABOUT PrEP COVERAGE?

- Each state has an insurance commissioner, often referred to as insurance regulators. State insurance regulators establish standards and best practices, conduct peer review, and coordinate their regulatory oversight while advocating for consumer protection. They serve as intermediaries between consumers and insurance companies. Individuals can reach out to their state insurance commissioners to request guidance on PrEP drug market changes.

NASTAD will continue to provide updates on the changing PrEP landscape. Sign up for NASTAD's PrEP Access mailing list to receive updates, and visit nastad.org/prepcost for additional resources.

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[1]"The Departments further clarify that under the 2015 Final Regulations and this IFC, plans and issuers subject to section 2713 of the PHS Act must cover, without cost sharing, items and services that are integral to the furnishing of the recommended preventive service, regardless of whether the item or service is billed separately. For example, several of the recommended preventive services involve screenings for the presence of certain health conditions, such as diabetes, or a variety of sexually transmitted infections. These recommended screenings, typically performed by laboratories, cannot be conducted without first collecting a specimen. Accordingly, plans and issuers subject to section 2713 of the PHS Act must cover without cost sharing both the specimen collection and the recommended preventive service, regardless of how the specimen collection is billed" (p. 122).

Department of Health and Human Services. (2020) Medicare and Medicaid IFC: Additional Policy and Regulatory Revisions in Response to the COVID-19 Public Health Emergency (CMS-9912-IFC). Centers for Medicare & Medicaid Services, Coronavirus waivers & flexibilities. Available at: https://www.cms.gov/files/document/covid-vax-ifc-4.pdf

[2]Current 340B drug pricing regulation has forced the manufacturer to provide deep 340B discounts to covered entities as a result of price increases that they have taken for Truvada since it was first approved for HIV treatment in 2004.