New high-cost HIV prevention drug: 'Better' isn't worth it

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A newly approved drug for HIV pre-exposure prophylaxis (PrEP) is unlikely to confer any discernible health benefit over generic alternatives and may undermine efforts to expand access to HIV prevention for the

nation's most vulnerable populations, according to a new study appearing today in the *Annals of Internal Medicine*.

The study, led by researchers at Massachusetts General Hospital (MGH) and the Yale School of Public Health, is also being released today at the Conference on Retroviruses and Opportunistic Infections in Boston, where top researchers from around the world will be discussing the ongoing battle against HIV/AIDS and related infectious diseases. The Harvard University Center for AIDS Research and the National Alliance of State and Territorial AIDS Directors were also collaborators on the research.

PrEP, a pill taken once a day, reduces the risk of HIV infection via sex or injection drug use by up to 99 percent. Since 2012, there has been one FDA-approved PrEP formulation: the combination of tenofovir/emtricitabine (F/TDF), marketed by Gilead Sciences and sold under the brand name Truvada. Patent protection for F/TDF is due to expire and the first generic version is expected in September 2020.

"F/TDF has a strong record of safety and efficacy," said Tim Horn, director, Medication Access and Pricing at the National Alliance of State & Territorial AIDS Directors and a study co-author. "The imminent arrival of a far cheaper, equally safe and effective, generic alternative is a golden opportunity to expand access to PrEP in some of the most difficult-to-reach segments of the at-risk population."

Complicating the roll-out of generic F/TDF is the arrival of a second PrEP agent: emtricitabine/tenofovir alafenamide (F/TAF), sold under the brand name Descovy and also marketed by Gilead. F/TAF was approved by the FDA in October 2019 for men who have sex with men (MSM) and transgender women, based on evidence of its "non-inferior" efficacy and lower impact on markers of bone and renal safety. Anticipating the entry of a generic competitor, Gilead has been moving

quickly to recommend that doctors switch patients to the new formulation, which it claims is considerably safer than F/TDF. Gilead's own projections are that it will succeed in transitioning as many as 45 percent of current patients on F/TDF for PrEP to branded F/TAF before F/TDF becomes generically available.

The study examined whether there was evidence to justify the rush to get patients to use the newly branded F/TAF. "How much is 'better' worth?" said lead author Rochelle P. Walensky, MD, MPH, chief, MGH Division of Infectious Diseases and a professor at the Harvard Medical School.

To answer that question, the researchers used data obtained from publicly available sources and recently completed clinical trials to evaluate the cost-effectiveness of F/TAF and to identify the highest possible price premium that branded F/TAF could command, even under the very best of circumstances, over generic F/TDF. To that end, the researchers intentionally overstated any adverse clinical and economic consequences of generic F/TDF, inflating rates of bone and renal disease incidence, assuming that all fractures would require surgical repair and that all cases of renal disease would require dialysis and be irreversible.

"Even when we cast branded F/TAF in the most favorable light possible, we found no plausible scenario under which F/TAF would be cost-effective compared to generic F/TDF, except perhaps for the vanishingly small number of persons with exceptionally high risk of bone or renal disease," Walensky said.

The researchers are quick to point out that while it is difficult to predict the price of generic F/TDF, it is unlikely to exceed $8,300 annually. Their analysis identifies a fair price markup over generic F/TDF of, at most, $670, suggesting that payors ought to be willing to pay no more than $8,970 for F/TAF, a price far below its current $16,600 market price.

"In the presence of a generic F/TDF option, branded F/TAF's price cannot be justified by its modest benefits," said study senior author A. David Paltiel, professor of public health (health policy) at the Yale School of Public Health. "If branded F/TAF succeeds in driving out its generic competitor, PrEP expansion in the US could grind to a halt and the new drug could end up causing more avoidable HIV transmissions than it prevents."

More information: *Annals of Internal Medicine* (2020). annals.org/errors/404.aspx?asp … doi/10.7326/M19-3478

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