HIV Treatment

TDF Versus TAF: What's the Difference?

Both tenofovir disoproxil fumarate (TDF) in Truvada and tenofovir alafenamide (TAF) in Descovy are highly effective and generally safe, but there are some important differences to be aware of.

Tenofovir is one of the most widely used medications for HIV and hepatitis B treatment; it is also approved for HIV pre-exposure prophylaxis (PrEP). Two forms of the drug are available: the older tenofovir disoproxil fumarate and the newer tenofovir alafenamide.

TAF is a prodrug that is absorbed more quickly than TDF and produces higher levels of the active drug, known as tenofovir diphosphate, in cells. This means it can be given in smaller doses, leading to lower drug levels in the blood and less exposure for the kidneys, bones and other organs.

First approved in 2001, TDF is sold as the stand-alone medication Viread and is a component of the combination pills Truvada, Atripla, Complera, Delstrigo, Stribild and Symfi/Symfi Lo. TDF is now off patent, and less expensive generic versions are available.

TAF, approved in 2015, is sold alone as Vemlidy and is a component of the combination pills Descovy, Biktarvy, Genvoya, Odefsey and Symtuza. TAF will remain under patent until 2022, and generic versions are not currently available.

Both TDF and TAF are included in the Department of Health and Human Services HIV guidelines as a recommended component of combination antiretroviral therapy. These medications must be used with other types of antiretrovirals for HIV treatment; using them alone can lead to drug resistance. Both medications, used alone, are also approved for hepatitis B virus (HBV) treatment.

Once-daily Truvada—which contains TDF—was the first drug approved, in 2012, for prevention of sexually acquired HIV. In 2019, the Food and Drug Administration (FDA) approved Descovy—which contains TAF—as a second PrEP option but not for sexual transmission via vaginal or frontal sex.

TDF is generally safe and well tolerated, but it can cause kidney problems and bone loss in some people. TAF has less effect on the kidneys and bones. On the other hand, TDF leads to lower cholesterol and triglyceride levels, which can lessen cardiovascular risk. TAF does not have the same beneficial effect on blood lipids, and it may be linked to greater weight gain.

An extensive body of research has compared people starting regimens that contain TDF with those starting TAF. Many other studies have looked at what happens when people switch from TDF to TAF—and, in a few cases, back to TDF again.

Treatment Effectiveness

Overall, research shows that both TDF and TAF are very effective for HIV treatment. Most people who take either TDF or TAF with modern integrase inhibitors, protease inhibitors or non-nucleoside reverse transcriptase inhibitors achieve an undetectable viral load. People who switch from TDF to TAF usually maintain viral suppression. Virological failure is uncommon with either TDF or TAF in people with good treatment adherence, and the two drugs have similar resistance profiles. Both lead to similar CD4 cell gains.

TDF and TAF are also similarly effective for hepatitis B treatment, resulting in high rates of viral suppression over years of follow-up.

Because TDF and TAF are both so effective, it is difficult to show whether one is statistically significantly better than the other. Clinical trials comparing the two drugs usually report that TAF is noninferior to TDF, meaning the drugs work about equally well.

Both TDF and TAF are generally safe and well tolerated. The most common side effects include headache, nausea and skin rash, which are usually mild to moderate. Severe adverse events are rare, and few people stop taking either drug because of side effects. But certain side effects warrant a closer look.

Kidney Problems

Tenofovir is eliminated from the body by the kidneys. The drug can damage tiny structures known as proximal tubules that are responsible for secreting waste products, reabsorbing water and maintaining stable blood chemistry.

Impaired kidney function can cause slower clearance of creatinine, a by-product of muscle metabolism. This leads to increased creatinine levels in the blood and a decrease in estimated glomerular filtration rate (eGFR); an eGFR measurement below 60 indicates moderate loss of kidney function. Other signs of impaired kidney function include low phosphate levels in the blood and protein in the urine.

Some people experience decreases in eGFR and other unfavorable changes in kidney biomarkers after starting TDF. These changes are usually small. Biomarkers often stabilize within several months after starting TDF, but some people continue to experience a gradual decline over time. Kidney problems are more likely when TDF is taken along with the booster drugs ritonavir or cobicistat. Major loss of kidney function is uncommon, however, and serious conditions like Fanconi syndrome (a type of kidney failure) are rare. People seldom have to stop taking TDF because of kidney-related problems.

In contrast, there is little or no change in eGFR or other kidney biomarkers after starting TAF. What's more, people who switch from TDF to TAF typically see an improvement in kidney function.

People with preexisting kidney problems, including an eGFR below 60, should not take Viread, Truvada or other coformulations containing TDF. Many experts recommend that people at risk for kidney problems should also avoid TDF. The risk of kidney problems rises with age. People living with HIV—especially African Americans—are more likely to have chronic kidney disease than HIV-negative people using PrEP. Some people who are unable to take TDF because of preexisting kidney disease or risk factors can safely use Vemlidy, Descovy and other TAF coformulations.

Bone Loss

Bone mineral density (BMD) is usually assessed by DEXA scans of the hip and spine. Certain biomarkers measured in the blood can also signal changes in bone production and reabsorption, collectively known as bone turnover.

Some people experience a decrease in bone density soon after starting TDF. Changes in blood chemistry resulting from impaired kidney function are thought to be the major cause of tenofovir-related bone loss, but the drug may also have direct effects on bone turnover.

Changes in BMD and bone biomarkers after starting TDF are usually small—around 1% to 3%—and often stabilize if people stay on the drug. It is not known whether these minor changes will eventually lead to clinical problems such as severe bone loss (osteoporosis) or fractures. However, most studies of TDF find that nontraumatic fractures (those attributable to bone loss rather than accidents or injuries) are uncommon.

Again, there is little or no change in DEXA scans or bone biomarkers after starting TAF. People who switch from TDF to TAF often see an improvement in markers of bone health.

People at higher risk for bone loss include those with existing osteoporosis and those with a history of fractures as well as older individuals, especially postmenopausal women. Some experts think TDF-related bone loss might be a bigger concern for children and adolescents, who still have developing bones.

Blood Fats and Weight Gain

People who start TDF often see decreases in total cholesterol, harmful LDL cholesterol and triglycerides. Some studies have shown modest weight loss as well. These changes are usually small, but they can be enough to bring some people under the level considered to be a high risk for cardiovascular disease and may allow some to stop taking lipid-lowering medications.

In contrast, starting TAF leads to little or no change in blood fat levels. People who switch from TDF to TAF often see a rise in total cholesterol, LDL and triglycerides. But beneficial HDL cholesterol may rise too, leaving the total cholesterol-to-HDL ratio unchanged. This may reflect lipids returning to pretreatment levels once the protective effect of TDF is gone, rather than being a direct effect

of TAF. These changes in blood lipids are reversible if people switch back to TDF.

A growing body of research shows that starting modern antiretroviral treatment is linked to weight gain. Some studies indicate that TAF-containing regimens are more likely to cause weight gain than those containing TDF or other drugs in its class, especially when combined with newer integrase inhibitors. Women and Black people—underrepresented in most clinical trials—appear more likely to gain weight. Research is under way to learn why this happens and whether it can be prevented.

TDF and TAF for PrEP

The large DISCOVER trial showed that both Truvada and Descovy are highly effective for prevention of sexually transmitted HIV among gay and bisexual men and transgender women. There were very few new cases of HIV among people who used either drug, and most of those were in individuals who did not appear to be taking PrEP consistently.

As with HIV treatment, Descovy for PrEP had less harmful effects on the kidneys and bones and a less beneficial effect on blood fats. But, on average, PrEP users are younger and healthier than people on HIV treatment, and serious kidney and bone problems were rare with either drug.

This study did not include cisgender (non-trans) women or transgender men, so the FDA did not approve Descovy PrEP for people who have vaginal or frontal sex until more evidence is available. Prior research has found that tenofovir reaches higher levels in rectal tissue compared with vaginal and cervical tissue in people who use TDF.

Because TAF produces higher tenofovir levels in cells and these levels are reached sooner and last longer, some experts have suggested that Descovy might offer more protection than Truvada for people who use on-demand, or 2-1-1, PrEP before and after sex (this dosing regimen is not FDA-approved for Truvada or Descovy). But this has not yet been tested in clinical trials.

The Bottom Line

TDF and TAF are both very effective for HIV and hepatitis B treatment as well as for PrEP. TAF and its coformulations are less likely to cause unfavorable changes in kidney and bone biomarkers, but serious kidney problems and bone loss are uncommon with either drug. TDF has the edge over TAF when it comes to blood fat levels and weight gain. TAF may be a better option for those at risk for kidney or bone problems, but both are safe options for most people.

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