Oscar Clinical Guideline: Descovy (emtricitabine/tenofovir alafenamide) (PG004, Ver. 6)

Descovy (emtricitabine/tenofovir alafenamide)

Summary

HIV (Human Immunodeficiency Virus) is a virus that attacks the immune system, leaving the body vulnerable to infections and diseases. It is primarily spread through sexual contact, sharing of needles or other injection equipment, or from mother to child during pregnancy, childbirth, or breastfeeding. There is currently no cure for HIV, but it can be managed with antiretroviral therapy (ART), which involves taking a combination of medications to suppress the virus and prevent the progression of HIV to AIDS. The specific combination of medications used in ART is tailored to the individual's needs and may depend on factors such as the person's overall health, the stage of the disease, and any other medical conditions they may have. Consideration of barriers to treatment, including social determinants of health, must also be carefully assessed for each patient to determine the most appropriate regimen tailored to their needs. ART is typically taken once or twice daily and may be adjusted over time as needed.

Pre-Exposure Prophylaxis (PrEP) is the use of is the use of anti-retroviral medications to prevent the acquisition of HIV. When taken consistently and correctly, PrEP can reduce the risk of HIV acquisition by over 99%. PrEP is not 100% effective and does not protect against other sexually transmitted infections (STIs). Therefore, condom use and frequent STI testing should be recommended PrEP is recommended for people who are at risk of acquiring HIV, particularly those who have multiple sexual partners, use

injection drugs, have a partner with HIV, or engage in condomless sex. PrEP is also recommended for people who are HIV-negative and are planning to become pregnant with an HIV-positive partner. The need for PrEP should be patient-driven, and offered to all patients who could benefit from its use.

Descovy is a fixed-dose combination of two antiretroviral drugs, emtricitabine and tenofovir alafenamide:

- used to treat HIV-1 infection in adults and adolescents who weigh at least 35 kg (77 lbs). Descovy is not a cure for HIV-1 infection and should be used in combination with other antiretroviral drugs. It is typically taken once daily with or without food. The dosage of Descovy may need to be adjusted in patients with kidney impairment.
- also approved for use in adults and adolescents weighing at least 35 kg who are at risk of HIV-1 infection through sexual acquisition, with the exception of individuals at risk from receptive vaginal sex. Prior to initiating Descovy for HIV-1 PrEP, individuals must have a negative HIV-1 test. It is important to note that the effectiveness of Descovy in individuals at risk of HIV-1 from receptive vaginal sex has not been sufficiently evaluated and is therefore not included in the approved indication.

Descovy tablets are available as:

- 200 mg/25 mg tablets each contain 200 mg of emtricitabine (FTC) and 25 mg of tenofovir alafenamide (TAF).
- 120 mg/15 mg tablets each contain 120 mg of FTC and 15 mg of TAF.

Definitions

"**Human Immunodeficiency Virus (HIV)**" is a virus that attacks the immune system, leaving the body vulnerable to infections and diseases. It is primarily spread through sexual contact, sharing of needles or other injection equipment, or from mother to child during pregnancy, childbirth, or breastfeeding.

"**Antiretroviral Therapy (ART)**" is the treatment for HIV that involves taking a combination of medications that work to suppress the virus and prevent it from replicating in the body. ART is not a cure for HIV, but it can significantly reduce the amount of virus in the body, slow the progression of the disease, and improve the immune system's function.

"**Pre-Exposure Prophylaxis (PrEP)**" is the use of anti-retroviral medications to prevent the acquisition of HIV.

"**Acquired Immune Deficiency Syndrome (AIDS)**" is an outdated term that was previously used to describe advanced HIV disease and the loss immune function required to fight certain infections.

Medical Necessity Criteria for Initial Authorization

The Plan considers **Descovy (emtricitabine/tenofovir alafenamide)** medically necessary when **ALL** the following criteria are met for the applicable indication listed below:

Treatment of HIV Infection

1. The member is at least 2 years of age and weighing at least 14 kg (31 lbs) or greater; ***AND***
2. The member has a documented diagnosis of human immunodeficiency virus type 1 (HIV-1) infection; ***AND***
3. Descovy is being prescribed for use in combination with other antiretroviral agent(s) as part of antiretroviral treatment (ART) regimen; ***AND***
4. The requested medication is being prescribed for use at the recommended dosage:
    a. members weighing 14 kg to less than 25 kg - one tablet containing 120 mg FTC and 15 mg TAF taken orally once daily; ***or***
    b. members weighing 25 kg or greater - one tablet containing 200 mg FTC and 25 mg of TAF taken orally once daily.

Preexposure Prophylaxis for Prevention of HIV-1 Infection

1. Descovy 200mg-25mg Tablet is being prescribed for pre-exposure prophylaxis (PrEP) for members meeting **ONE** of the following criteria:
    a. to reduce the risk of sexually acquired HIV-1 (i.e., those with an HIV-positive sexual partner, recent sexually transmitted infection, multiple sex partners, history of inconsistent or no condom use, commercial sex work or transactional sex, in high-prevalence area or network); ***or***
    b. injection drug users at substantial risk of HIV acquisition (i.e., those with an HIV-positive injecting partner and those sharing injection equipment or who recently received drug treatment but are currently injecting); ***AND***
2. The member is documented to be HIV-1-negative; ***AND***
3. The member must be unable to use, or have a documented clinical rationale indicating they are not an appropriate candidate (e.g. baseline renal dysfunction or at risk for developing renal impairment, osteoporosis, low bone mineral density, or at risk of developing low bone mineral density) for emtricitabine and tenofovir disoproxil fumarate (Truvada).

If the above prior authorization criteria is met, Descovy (emtricitabine/tenofovir alafenamide) will be approved for 12 months.

Medical Necessity Criteria for Reauthorization

Reauthorization for 12 months will be granted if **BOTH** of the following are met:

1. the member still meets the applicable initial criteria***; AND***
2. recent chart documentation (within the last 6 months) shows the member has experienced therapeutic response to the requested medication as evidenced by **ONE** of the following:
    a. Treatment of HIV Infection - achieve and maintain viral suppression***; or***
    b. Preexposure Prophylaxis for Prevention of HIV-1 Infection - a documented negative HIV test.

Experimental or Investigational / Not Medically Necessary

Descovy (emtricitabine/tenofovir alafenamide) for any other indication is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven.

Appendix

TDF-FTC vs. TAF-FTC for Pre-Exposure Prophylaxis (PrEP): Safety, Efficacy, and Clinical Considerations

Pre-exposure prophylaxis (PrEP) is a critical HIV prevention strategy for high-risk individuals, but its use requires careful considerations and precautions. The fixed combinations of emtricitabine/TDF (FTC-TDF) and emtricitabine/TAF (FTC-TAF) are FDA-approved for PrEP in conjunction with safer sex practices for at-risk HIV-1-negative adults and adolescents weighing 35 kg or more. Efficacy and safety of these regimens have been demonstrated in multiple clinical trials, and their effectiveness is strongly correlated with adherence.

- NOTE: TAF-FTC is not approved for PrEP in women at risk for acquiring HIV infection from receptive vaginal sex because its effectiveness has not been evaluated in this situation, and it is not recommended in the 2021 CDC guideline for this population.

Oral PrEP with TDF or TDF-FTC has been shown to decrease the risk of acquiring HIV infection compared to placebo or no PrEP. The absolute difference in risk of HIV infection was about 2%, with a number needed to treat of about 50 to prevent one case of HIV infection. In three trials involving MSM, the pooled absolute difference was larger at about 5%, with a number needed to treat of about 20. Effects of PrEP on HIV infection risk were similar for TDF alone and TDF-FTC. However, TDF alone is not FDA-approved for use as PrEP and is no longer recommended in the 2021 CDC guideline.

A strong association was found between study-level adherence and estimates of effectiveness. In six trials with adherence of 70% or greater, the pooled RR was 0.27, with no statistical heterogeneity. The DISCOVER trial found oral daily TAF-FTC to be noninferior to TDF-FTC for incident HIV infection in primarily MSM and potentially associated with increased efficacy. TAF-FTC showed positive short-term effects on bone mineral density and negative effects on lipid parameters and weight gain, without differences in clinical adverse events, including renal events and fractures.

The use of FTC-TDF for PrEP is considered non-inferior to FTC-TAF, with a few exceptions where FTC-TAF may be more appropriate. The 2021 CDC Guidelines for PrEP recommend daily oral FTC-TDF or FTC-TAF for men and transgender women but exclude cisgender women at risk through receptive vaginal sex. Both FTC-TDF and FTC-TAF have shown similar safety and effectiveness in reducing the risk of sexual HIV acquisition, and no differences in clinically meaningful adverse events have been observed. However, renal function and bone health should be considered when prescribing these medications.

The DISCOVER trial found no significant differences between FTC-TAF and FTC-TDF in the risk of serious adverse events, discontinuation due to adverse events, or any adverse event. Renal adverse event rates were also similar, but FTC-TAF was associated with a greater percent change from baseline in hip bone mineral density for individuals aged 25 years or older.

Current clinical practice and recommendations from other groups, such as the US Public Health Service and the International Antiviral Society-USA, recommend PrEP with FTC-TDF for adults at high risk of infection. FTC-TAF is recommended for men who have sex with men (MSM) with or at risk for kidney dysfunction, osteopenia, or osteoporosis. Injectable cabotegravir is recommended as an alternative option for cisgender men and transgender women who have sex with men.

Table 1: Summary of Clinical Review and Recommendations from Various Sources

Source	Summary of Findings
Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults: 2020 Recommendations of the International Antiviral Society–USA Panel	This panel supports the use of both TDF/FTC and TAF/FTC for PrEP in appropriate populations. They recognize that TAF/FTC has a more favorable renal and bone safety profile compared to TDF/FTC.
The Centers for Disease Control and Prevention (CDC) PrEP Guidelines	According to the CDC, both TDF/FTC and TAF/FTC are recommended as PrEP options for at-risk populations. TDF/FTC is recommended for all individuals at risk, including cisgender men and women, transgender women, and men who have sex with men. TAF/FTC is recommended for cisgender men, transgender women,

	and men who have sex with men but is not recommended for cisgender women or individuals at risk for HIV due to injection drug use.
The Department of Health and Human Services (DHHS) Guidelines	The Department of Health and Human Services (DHHS) guidelines recommend TDF/FTC for all individuals at risk for HIV, while TAF/FTC is recommended for men who have sex with men and transgender women, but not for cisgender women or individuals at risk due to injection drug use.
DISCOVER Trial	The DISCOVER trial was a phase 3, randomized, double-blind, multicenter, active-controlled study comparing the safety and efficacy of TDF/FTC and TAF/FTC in men and transgender women who have sex with men (MSM and TGW) for HIV PrEP. The trial found that TAF/FTC was non-inferior to TDF/FTC in preventing HIV infection, with a similar overall safety profile.
The U.S. Preventive Services Task Force (USPSTF) Recommendations	The U.S. Preventive Services Task Force (USPSTF) recommends offering PrEP with TDF/FTC or TAF/FTC to persons at high risk of HIV acquisition. Both options are considered safe and effective for preventing HIV infection.

Plan Position Statement

TDF/FTC and TAF/FTC are equally appropriate options in clinical practice for pre-exposure prophylaxis (PrEP) in preventing HIV infection. Both TDF/FTC and TAF/FTC have equivalent high efficacy and safety as PrEP in clinical trials and are supported by recommendations from major health organizations.

1. There is usually no need to switch from TDF/FTC to TAF/FTC. While some studies have shown differences in laboratory markers of bone metabolism and renal function, no differences in clinically meaningful adverse events have been observed. TAF/FTC is indicated for patients with estimated creatinine clearance (eCrCl) <60 ml/min but ≥30 ml/min, while either TDF/FTC or TAF/FTC can be used when eCrCl ≥60 ml/min. Clinicians may prefer TAF/FTC for persons with previously documented osteoporosis or related bone disease, but routine screening for bone density is not recommended for PrEP patients.
2. Renal function must be assessed before starting PrEP with either TDF/FTC or TAF/FTC, as decreased renal function is a potential safety issue. Small decreases in renal function have been observed with TDF/FTC PrEP use, which mostly reversed when PrEP was discontinued. In the DISCOVER trial comparing TDF/FTC and TAF/FTC for PrEP, no difference in clinically important renal health measures was observed, but some biochemical markers of proximal tubular function

favored TAF/FTC. This may indicate a longer-term safety benefit for men with pre-existing risk factors for renal dysfunction.

3. In the DISCOVER trial, higher rates of triglyceride elevation and weight gain were seen among men taking TAF/FTC than among men taking TDF/FTC. TDF/FTC has been associated with reductions in HDL and LDL cholesterol that are not seen with TAF/FTC. This may indicate a longer-term safety risk when prescribing TAF/FTC PrEP for men with pre-existing cardiovascular health risk factors. All persons prescribed TAF/FTC for PrEP should have monitoring of triglyceride and cholesterol levels every 12 months, with lipid-lowering medications prescribed when indicated.

References

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