emtricitabine/tenofovir alafenamide (Descovy®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO188

Description

Emtricitabine/tenofovir alafenamide (Descovy®) is a two-drug combination of emtricitabine (FTC) 200 mg and tenofovir alafenamide (TAF) 25 mg. Emtricitabine 5' triphosphate inhibits the activity of the HIV-1 reverse transcriptase and tenofovir diphosphate inhibits HIV-1 replication through incorporation into viral DNA.

Length of Authorization

- Initial: 12 months
- Renewal: 12 months

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit
emtricitabine/tenofovir alafenamide (Descovy)	Pre-Exposure Prophylaxis (PrEP); Treatment of HIV-1	200-25 mg tablets	30 tablets/30 days
	Treatment of HIV-1	120-15 mg tablets	

Initial Evaluation

I. **Emtricitabine/tenofovir alafenamide (Descovy)** may be considered medically necessary when the following criteria are met:
   A. A diagnosis of the following:
      1. A diagnosis of **HIV-1** and the following is met:
         i. Medication is prescribed by, or in consultation with, an infectious disease or HIV specialist; **AND**
         ii. Member's bodyweight is 14-16kg; **OR**
         iii. Member's bodyweight is 17kg (37.5lbs) or greater; **AND**
            a. Documentation that the member is not a candidate for a generic tenofovir disoproxil fumarate-based regimen due to contraindication or intolerance defined by any one of the following**:**
               i. Requires renal hemodialysis; **OR**
               ii. Stabilized creatinine clearance (CrCl) less than 59 ml/min within the prior 3 months; **OR**
               iii. Stabilized creatinine clearance (CrCl) between 60-89 mL/min; **AND**

1. Member has hypertension; **AND**
2. Member has one of the following:
    a. Diabetes
    b. Hepatitis C
    c. Vascular kidney disease (e.g., renal artery stenosis)
    d. Structural abnormalities (e.g., polycystic kidney, dysplastic kidney, renal mass)
    e. Member is African American with a family history of kidney disease; **OR**

iv. Member is high risk for bone complications as determined by a history of one of the following:
1. Vertebral compression factor
2. Arm or hip fracture with minimal trauma
3. Member has chronic kidney disease with proteinuria, low phosphate, or is grade 3 or worse
4. T score, less than, or equal to, -2.0 (DXA) at the femoral neck or spine
5. Chronic, high dose glucocorticoid-therapy defined as more than 5 mg/day of prednisone, or equivalent, daily; **AND**
    a. Member has ongoing use of glucocorticoid therapy; **AND**
    b. Documentation of the member's current glucocorticoid regimen; **AND**
    c. The expected duration of glucocorticoid therapy is greater than 2 months**; OR**

2. Medication will be used in the setting of **Pre-Exposure Prophylaxis (PrEP)** when the following are met:
    i. Member is at high risk for acquiring HIV-1 infection from sexual acquisition (e.g., engaging in sexual activity with a HIV-1 infected partner, multiple diagnosis of sexually transmitted infections); **AND**
    ii. Member has a negative HIV-1 test no more than seven days prior to initiating treatment; **AND**
    iii. Member's body weight is greater than, or equal to, 35 kg (77lbs); **AND**
    iv. Documentation that the member is not a candidate for generic emtricitabine/tenofovir disoproxil fumarate due to any one of the following:
        a. Requires renal hemodialysis; **OR**

b. Stabilized creatinine clearance (CrCl) less than 60 mL/min within the prior 3 months; **OR**
c. Member has experienced significant adverse effects to emtricitabine/tenofovir disoproxil fumarate; **AND**
    i. Documentation that adverse effects significantly impact adherence or quality of life; **AND**
    ii. Documentation that adverse effects resolved upon drug discontinuation

II. Emtricitabine/tenofovir alafenamide (Descovy) is considered not medically necessary when criteria above are not met and/or when used for:
    A. Prevention of HIV in adults and adolescents not at risk of HIV-1 infection from sexual acquisition

III. Emtricitabine/tenofovir alafenamide (Descovy) is considered investigational when used for all other conditions, including but not limited to:
    A. Use for prevention of other sexually transmitted diseases (STI's)

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. A diagnosis of one of the following:
    A. **HIV-1**; **AND**
        1. Member's condition has not worsened while on therapy as evidenced by one of the following:
            i. A viral load less than 200 copies/mL; **OR**
            ii. An increasing CD4 cell count; **OR**
    B. Medication will be used in the setting of **Pre-Exposure Prophylaxis (PrEP); AND**
        a. Member is at high risk for acquiring HIV-1 infection from sexual acquisition (e.g., engaging in sexual activity with a HIV-1 infected partner, multiple diagnosis of sexually transmitted infections); **AND**
        b. Member has had a negative HIV-1 test within the last 3 months; **AND**
        c. Documentation that the member is not a candidate for generic emtricitabine/tenofovir disoproxil fumarate due to any one of the following:
            i. Requires renal hemodialysis; **OR**

ii. Stabilized creatinine clearance (CrCl) less than 60 mL/min within the prior 3 months; **OR**
iii. Member has experienced significant adverse effects to emtricitabine/tenofovir disoproxil fumarate; **AND**
    1. Documentation that adverse effects significantly impact adherence or quality of life; **AND**
    2. Documentation that adverse effects resolved upon drug discontinuation

Supporting Evidence

HIV-1

I. Due to the ongoing and complex nature of treating those that are HIV-1 positive, it is important this medication is only prescribed by those that are trained in infectious diseases or specializes in HIV treatment.
II. Safety and efficacy of emtricitabine/tenofovir alafenamide (Descovy) has been established in seven clinical trials in patients with a diagnosis of HIV-1.
    - From those seven clinical trials two were randomized, double-blind, active-controlled, Phase 3 studies in HIV-1 infected treatment naïve adults (Study 104 and Study 111) where patients received E/C/F/TAF or E/C/F/TDF or placebo.
        - The primary endpoint was percentage of participants with HIV-1 RNA < 50 Copies/mL. E/C/F/TAF was non-inferior to E/C/F/TDF for the combined primary outcome (800 patients [92%] vs 784 patients [90%], adjusted difference 2.0%, 95% CI −0.7% to 4.7%).
        - Secondary endpoint of mean increases from baseline in CD4 cell counts was higher for the E/C/F/TAF through week 48 (E/C/F/TAF 230 (SD 177.3) cells/mL; E/C/F/TDF 211 (170.7) cells/mL) with a difference in LSM 19 cells/mL, 95% CI: 3-36 cells/mL; p=0.024.
    - Study 109 was a randomized, open-label, active-controlled, noninferiority study in HIV-1 infected virologically suppressed adults who received FTC+TAF with elvitegravir, cobicistat, emtricitabine, and TAF - E/C/F/TAF (TAF group) or emtricitabine, TDF, atazanavir, and cobicistat (COBI) or ritonavir or FTC+TDF with elvitegravir +COBI (TDF group).
        - The primary endpoint was percentage of participants with HIV-1 RNA < 50 copies/mL. Of patients previously on elvitegravir, cobicistat, emtricitabine, and TDF before randomization, 98% of those who switched to TAF maintained virological control, compared to the 97% who continued their regimen (percentage difference 1.0%; 95% CI −1.9 to 3.9).
        - Secondary endpoint: Mean Bone Mineral Density (BMD) at the hip and spine increased in the TAF group while remaining stable or decreasing in the TDF group (p<0.0001). Hip

and spine BMD improved in patients assigned to the TAF group compared with the TDF group, irrespective of previous treatment.

- T-score BMD for both hip and spine increased in patients assigned to the TAF group, while remaining stable in those who continued their initial TDF based regimen. A greater number of patients in the TAF group than in the TDF group recovered from osteopenia or osteoporosis at either the hip or the spine during the 48 weeks ($p<0.0001$).
- Additional secondary endpoint was change from baseline in serum creatinine in those assigned to the TDF group compared with the TAF group (2.9 µmol/L [SD 9.29] vs −0.4 µmol/L [10.14] in the TAF group; difference in least squares mean for TAF group vs TDF group was −3.33 µmol/L [95% CI −4.57 to −2.10 µmol/L] ($p<0·0001$).

- Study 112 was an open-label trial that looked at HIV-1 infected virologically suppressed adults with renal impairment (estimated creatinine clearance between 30 and 69 mL/min. The study included 242 adults on 150 mg elvitegravir, 150 mg cobicistat, 200 mg FTC, and 10 mg TAF (E/C/F/TAF).
  - The primary outcomes were change from baseline in the estimated glomerular filtration rate (eGFR). Through the 48 weeks there was no clinically appreciable change from baseline in estimated creatinine clearance observed, with direction and magnitude varying by filtration marker and equation. Results were similar for patients whether baseline eGFR was <50 or ≥50 mL/min or whether they switched from a TDF-based regimen.
  - The prevalence of significant proteinuria (UPCR > 200 mg/g) and albuminuria (UACR ≥ 30 mg/g) decreased from 42% to 11% and from 49% to 21%, respectively.
  - BMD significantly increased after switch to E/C/F/TAF for patients on a TDF-containing regimen pre-switch and remained stable after switch to E/C/F/TAF for patients on non-TDF-containing regimen pre-switch. Mean percent changes from baseline to week 48 in hip and spine BMDs significantly increased (+1.47% and +2.29%, respectively), and more patients had significant (≥3%) gains in hip or spine BMD than those who had significant loss.

III. Emtricitabine/tenofovir alafenamide (Descovy) is not recommended in patients with estimated creatinine clearance below 15 to below 30 mL/min, or in individuals with estimated creatinine clearance below 15 mL/min who are not receiving chronic hemodialysis.

IV. Stage two CKD is defined by a GFR between 60-89 mL/min for three months or longer along with kidney damage.

V. Emtricitabine/tenofovir alafenamide (Descovy) is not approved in the treatment of chronic HBV infection as the safety and efficacy has not yet been established in patients who are coinfected with HIV-1 and HBV. As severe acute exacerbations of hepatitis B (e.g., liver decompensation and liver failure) have been reported in patients who are coinfected with HIV-1 and HBV who have discontinued products containing FTC and/or TDF and may occur when

emtricitabine/tenofovir alafenamide (Descovy) is discontinued. Due to this, patients who are coinfected with HIV-1 and HBV who have discontinued emtricitabine/tenofovir alafenamide (Descovy) should be closely monitored with both clinical and laboratory follow-up.

VI. No dosage adjustment of emtricitabine/tenofovir alafenamide (Descovy) is recommended in patients with mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment as emtricitabine/tenofovir alafenamide (Descovy) has not been studied in patients with severe hepatic impairment (Child-Pugh Class C).

VII. Estimated creatinine clearance, urine glucose, and urine protein should be assessed before initiating emtricitabine/tenofovir alafenamide (Descovy) therapy and should be monitored during therapy in all patients. Serum phosphorus should be monitored in patients with chronic kidney disease as these patients are at higher risk of developing Fanconi syndrome on tenofovir prodrugs. Emtricitabine/tenofovir alafenamide (Descovy) should be discontinued in patients who develop clinically significant decreases in renal function or evidence of Fanconi syndrome.

VIII. No safety or efficacy data is available in patients with renal impairment who received emtricitabine/tenofovir disoproxil fumarate (Truvada) using these dosing guidelines, so the potential benefit of emtricitabine/tenofovir disoproxil fumarate (Truvada) therapy should be assessed against the potential risk of renal toxicity. Emtricitabine/tenofovir disoproxil fumarate (Truvada) is not recommended in patients with estimated creatinine clearance below 30 mL/min or patients requiring hemodialysis.

IX. In clinical trials in HIV-1 infected treatment-naïve adults a significant decline in BMD was observed in 15% of subjects treated with FTC+TAF with EVG+COBI. However, as the long-term clinical significance of these changes has not been established, assessment of BMD should be considered for adults and pediatric patients treated with emtricitabine/tenofovir alafenamide (Descovy) who have a history of pathologic bone fracture or other risk factors for osteoporosis or bone loss. Calcium and vitamin D supplementation may be beneficial for all patients and should be considered. Cases of osteomalacia associated with proximal renal tubulopathy, manifested as bone pain or pain in extremities and which may contribute to fractures, have been reported in association with the use of TDF-containing products. Hypophosphatemia and osteomalacia secondary to PRT have occurred in patients who are at risk of renal dysfunction who present with persistent or worsening bone or muscle symptoms while receiving products containing TDF. However, as this was not studied in clinical studies of emtricitabine/tenofovir alafenamide (Descovy), the risk of osteomalacia with emtricitabine/tenofovir alafenamide (Descovy) is not known.

X. The efficacy and safety of emtricitabine/tenofovir alafenamide (Descovy), used in combination with other antiretroviral agents for the treatment of HIV-1 infection, was established in pediatric patients 12 years of age and older who had a body weight greater than, or equal to, 35 kg. Use of emtricitabine/tenofovir alafenamide (Descovy) in this age group is supported by adequate and well controlled studies of FTC+TAF with EVG+COBI in adults and by a 24-week open label trial of 23 antiretroviral treatment-naïve HIV-1 infected pediatric subjects, aged 12-18 years old,

weighing at least 35 kg, and who were treated with FTC+TAF with EVG+COBI. The safety and efficacy of FTC+TAF with EVG+COBI was similar to that of antiretroviral treatment-naïve HIV-1 infected adults on this same regimen.

XI. Use of emtricitabine/tenofovir alafenamide (Descovy) in pediatric patients aged two to less than six years of age and weighing at least 14 to less than 25kg is supported by an open-label trial of FTC+TAF with bictegravir (N=22; cohort 3) in virologically suppressed pediatric patients and studies of FTC+TAF with EVG+COBI in adults. The safety and efficacy of FTC+TAF in these pediatric patients were similar to that observed in adults who received FTC+TAF with bictegravir. Emtricitabine/tenofovir disoproxil fumarate (Truvada) has been studied in pediatric patients weighing ≥17kg only. Patients weighing 14kg to less than 17kg are not candidates for emtricitabine/tenofovir disoproxil fumarate (Truvada) as efficacy and safety of emtricitabine/tenofovir disoproxil fumarate (Truvada) has not been established in this population.

XII. In clinical trials, 80 of the 97 subjects enrolled were 65 years and over and received FTC+TAF and EVG+COBI, with no differences in safety or efficacy being observed between elderly subjects and those between 12 and 65 years of age.

PrEP

XIII. The efficacy and safety of emtricitabine/tenofovir alafenamide (Descovy) to reduce the risk of acquiring HIV-1 infection were studied in a randomized, double-blind, active-controlled multinational trial (DISCOVER) in HIV-seronegative men (N=5,262) or transgender women (N=73) who have sex with men and are at risk for HIV-1 infection. Subjects were included in the trial if they met criteria for high-risk behavior defined as one of the following: two or more unique condomless anal sex partners in the past 12 weeks or a diagnosis of rectal gonorrhea/chlamydia or syphilis in the past 24 weeks. Clinical trial compared the incidence of documented HIV-1 infection per 100 person-years in participants randomized to once daily emtricitabine/tenofovir alafenamide (Descovy) and emtricitabine/tenofovir disoproxil fumarate (Truvada) and found that study drug was non-inferior to comparator at reducing the risk of acquiring HIV-infection with rate ratio of 0.468 [95% CI, 0.19, 1.15].

XIV. The FDA HIV-1 PrEP indication for emtricitabine/tenofovir alafenamide (Descovy) does not include individuals at risk of HIV-1 from receptive vaginal sex; however, there are preliminary pharmacokinetic data in healthy, non-pregnant, HIV negative, premenopausal (aged 18-50) cis-gender women evaluated in a Phase 1 clinical trial (NCT02904369). Results demonstrate that participants had higher tenofovir-diphosphate (TVF-DP) levels in peripheral blood mononuclear cells (PBMCs) with tenofovir alafenamide (TAF) than with tenofovir disoproxil fumarate (TDF), suggesting emtricitabine/tenofovir alafenamide (Descovy) should be just as effective in preventing HIV-infections in this population. No new safety concerns were reported with the TAF formulation. Thus, emtricitabine/tenofovir alafenamide (Descovy) is expected to produce similar results as emtricitabine/tenofovir disoproxil fumarate (Truvada) in this population. Use

of emtricitabine/tenofovir disoproxil fumarate (Truvada) in cis-gender women is supported by a randomized, double-blind, placebo-controlled Partners PrEP study.

XV. Per Center for Disease Control (CDC) guidelines, while on PrEP, a person is advised to also get periodic HIV and STD testing. CDC recommends documenting a negative HIV test result within the week before initiating (or reinitiating) PrEP medications, ideally with an antigen/antibody test conducted by a laboratory. For patient safety, HIV testing should be repeated at least every three months after oral PrEP initiation. If the person acquires HIV while taking PrEP, they must immediately be provided a full antiretroviral therapy (ART) regimen to prevent drug resistance.

XVI. The safety and efficacy of emtricitabine/tenofovir alafenamide (Descovy) for prevention of HIV-1 infection has not been evaluated in patients weighing <35kg (77lbs). At this time, emtricitabine/tenofovir alafenamide (Descovy) is only indicated in at-risk adults and adolescents weighing at least 35kg for PrEP.

XVII. Emtricitabine/tenofovir disoproxil fumarate (Truvada) is FDA approved for PrEP in healthy adults and adolescents at risk for acquiring HIV-1 infection and continues to be the most commonly prescribed oral medication for those meeting criteria for PrEP use. There are no clinically meaningful efficacy or safety differences between emtricitabine/tenofovir disoproxil fumarate (Truvada) and emtricitabine/tenofovir alafenamide (Descovy). At this time, generic emtricitabine/tenofovir disoproxil fumarate (Truvada) remains the most cost-effective agent and in the absence of contraindications is required to be trialed first. Contraindications to the use of emtricitabine/tenofovir disoproxil fumarate (Truvada) for HIV-1 PrEP include individuals with estimated creatinine clearance below 60mL/min or those requiring hemodialysis. Relative contraindications additionally include those previously treated with emtricitabine/tenofovir disoproxil fumarate (Truvada) and experiencing adverse reactions related to the drug such that adverse reactions impacted adherence and/or quality of life and led to drug discontinuation.

XVIII. For those established on emtricitabine/tenofovir alafenamide (Descovy) through a previous health plan, medical necessity requirements for use of brand Descovy over use of generic of emtricitabine/tenofovir disoproxil fumarate remain required.

XIX. Clinically significant bone mineral density (BMD) changes have not been observed in clinical trials studying emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP. A 3%-4% decline in BMD was seen in HIV-infected persons treated with combination antiretroviral therapy; however, it is unclear whether a similar decline would be seen in HIV-uninfected persons taking fewer antiretroviral medications for PrEP. At this time, clinical guidelines do not recommend DEXA scans or other assessments of bone health before initiation of PrEP or for monitoring of persons while taking PrEP. Therefore, decreased bone mineral density is not considered a contraindication to treatment with emtricitabine/tenofovir disoproxil fumarate at this time.

Investigational or Not Medically Necessary Uses

I. Emtricitabine/tenofovir alafenamide (Descovy) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. Prevention of HIV in adults and adolescents not at risk of HIV-1 infection from sexual acquisition
   B. Use as a cure for those HIV-1 positive
   C. Use as a preventive measure against other STI's

References

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Policy Implementation/Update:

Action and Summary of Changes	Date
Removed specialist requirement in the setting of PrEP.	06/2023
Updated initial duration to 12 months from 3 months	12/2022
Updated renewal criteria to allow a path to coverage for those established through a previous health plan. Updated PrEP renewal criteria to require use of generic Truvada. Updated supporting evidence section.	08/2022
Included new Descovy strength (120-15mg tablets); updated HIV-1 initial criteria to expand use in pediatric patients weighing between 14 and 16kg; updated HIV-1 indication weight criterion from 25kg to 17kg to align with Truvada's label, added/defined additional contraindications to generic Truvada in the setting of PrEP, removed criteria requiring use in adults at risk from receptive vaginal sex from PrEP, defined HIV-1 testing requirement frequency in the renewal section for PrEP, updated supporting evidence sections.	05/2022
Policy created	12/2020