DESCOVY- emtricitabine and tenofovir alafenamide tablet
Gilead Sciences, Inc.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use DESCOVY safely and effectively. See full prescribing information for DESCOVY.

DESCOVY® (emtricitabine and tenofovir alafenamide) tablets, for oral use
Initial U.S. Approval: 2015

WARNING: POST-TREATMENT ACUTE EXACERBATION OF HEPATITIS B and RISK OF DRUG RESISTANCE WITH USE OF DESCOVY FOR HIV-1 PRE-EXPOSURE PROPHYLAXIS (PrEP) IN UNDIAGNOSED EARLY HIV-1 INFECTION

See full prescribing information for complete boxed warning.

Severe acute exacerbations of hepatitis B (HBV) have been reported in individuals with HBV who have discontinued products containing emtricitabine (FTC) and/or tenofovir disoproxil fumarate (TDF), and may occur with discontinuation of DESCOVY. Hepatic function should be monitored closely in these individuals. If appropriate, anti-hepatitis B therapy may be warranted. (5.1)

DESCOVY used for HIV-1 PrEP must only be prescribed to individuals confirmed to be HIV-negative immediately prior to initiating and at least every 3 months during use. Drug-resistant HIV-1 variants have been identified with use of FTC/TDF for HIV-1 PrEP following undetected acute HIV-1 infection. Do not initiate DESCOVY for HIV-1 PrEP if signs or symptoms of acute HIV-1 infection are present unless negative infection status is confirmed. (5.2)

RECENT MAJOR CHANGES

Indications and Usage (1.1)	06/2025
Dosage and Administration, Recommended Dosage for Treatment of HIV-1 Infection in Pediatric Patients Weighing at Least 14 kg to Less than 35 kg (2.4)	06/2025

INDICATIONS AND USAGE

HIV-1 Treatment (1.1):
DESCOVY is a two-drug combination of emtricitabine (FTC) and tenofovir alafenamide (TAF), both HIV nucleoside analog reverse transcriptase inhibitors (NRTIs), and is indicated:

- in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and adolescent patients weighing at least 35 kg.
- for the treatment of HIV-1 infection in pediatric patients weighing at least 14 kg to less than 35 kg in combination with other antiretroviral agents, including darunavir and cobicistat but not other protease inhibitors that require a CYP3A inhibitor.

HIV-1 PrEP (1.2):
DESCOVY is indicated in at-risk adults and adolescents weighing at least 35 kg for pre-exposure prophylaxis (PrEP) to reduce the risk of HIV-1 infection from sexual acquisition, excluding individuals at risk from receptive vaginal sex. Individuals must have a negative HIV-1 test immediately prior to initiating DESCOVY for HIV-1 PrEP.
Limitations of Use (1.2):
The indication does not include use of DESCOVY in individuals at risk of HIV-1 from receptive vaginal sex because effectiveness in this population has not been evaluated.

DOSAGE AND ADMINISTRATION

- Testing: Prior to or when initiating DESCOVY, test for hepatitis B virus infection. Prior to or when initiating DESCOVY, and during use on a clinically appropriate schedule, assess serum creatinine, estimated creatinine clearance, urine glucose, and urine protein in all individuals. In individuals with chronic kidney disease, also assess serum phosphorus. (2.1)
- HIV-1 Screening: Screen all individuals for HIV-1 infection immediately prior to initiating DESCOVY for

HIV-1 PrEP and at least once every 3 months while taking DESCOVY, and upon diagnosis of any other sexually transmitted infections (STIs). (2.2)

- Recommended dosage:
  - Treatment of HIV-1 Infection:
    - Adult and pediatric patients weighing at least 35 kg: One 200 mg/25 mg tablet once daily with or without food. (2.3)
    - Pediatric patients receiving DESCOVY with other antiretroviral agents, including darunavir and cobicistat but not other protease inhibitors administered with either ritonavir or cobicistat, and weighing:
      - at least 25 to less than 35 kg: One 200 mg/25 mg tablet once daily with or without food. (2.4)
      - at least 14 to less than 25 kg: One 120 mg/15 mg tablet once daily with or without food. (2.4)
  - HIV-1 PrEP: One 200 mg/25 mg tablet once daily with or without food in individuals with body weight at least 35 kg. (2.5)
- Renal impairment: DESCOVY is not recommended in individuals with estimated creatinine clearance of 15 to below 30 mL per minute, or below 15 mL per minute who are not receiving chronic hemodialysis. (2.6)

DOSAGE FORMS AND STRENGTHS

Tablets: 200 mg/25 mg and 120 mg/15 mg of FTC and TAF respectively (3)

CONTRAINDICATIONS

DESCOVY for HIV-1 PrEP is contraindicated in individuals with unknown or positive HIV-1 status. (4)

WARNINGS AND PRECAUTIONS

- Comprehensive management to reduce the risk of sexually transmitted infections (STIs), including HIV-1, when DESCOVY is used for HIV-1 PrEP: Counsel on adherence to daily dosing and safer sex practices, including condoms, to reduce the risk of STIs. (5.2)
- Management to reduce the risk of acquiring HIV-1 drug resistance when DESCOVY is used for HIV-1 PrEP: refer to full prescribing information for additional detail. (5.2)
- Immune reconstitution syndrome during treatment of HIV-1 infection: May necessitate further evaluation and treatment. (5.3)
- New onset or worsening renal impairment: Assess serum creatinine, estimated creatinine clearance, urine glucose, and urine protein when initiating DESCOVY and during use on a clinically appropriate schedule in all individuals. Also assess serum phosphorus in individuals with chronic kidney disease. (5.4)
- Lactic acidosis/severe hepatomegaly with steatosis: Discontinue DESCOVY in individuals who develop symptoms or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity. (5.5)

ADVERSE REACTIONS

- In participants with HIV-1, the most common adverse reaction (incidence greater than or equal to 10%, all grades) was nausea. (6.1)
- In adults without HIV-1 in a PrEP trial, the most common adverse reaction (incidence greater than or equal to 5%, all grades) was diarrhea. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Gilead Sciences, Inc. at 1-800-GILEAD-5 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Consult the Full Prescribing Information prior to and during use for potential drug interactions. (7, 12.3)

USE IN SPECIFIC POPULATIONS

- Pediatrics:
  - Treatment of HIV-1 Infection: Not recommended for patients weighing less than 14 kg. (8.4)
  - HIV-1 PrEP: Not recommended for individuals weighing less than 35 kg. (8.4)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 7/2026

FULL PRESCRIBING INFORMATION: CONTENTS*

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FULL PRESCRIBING INFORMATION

WARNING: POST-TREATMENT ACUTE EXACERBATION OF HEPATITIS B and RISK OF DRUG RESISTANCE WITH USE OF DESCOVY FOR HIV-1 PRE-EXPOSURE PROPHYLAXIS (PrEP) IN UNDIAGNOSED EARLY HIV-1 INFECTION

Severe acute exacerbations of hepatitis B (HBV) have been reported in individuals with HBV who have discontinued products containing emtricitabine (FTC) and/or tenofovir disoproxil fumarate (TDF) and may occur with discontinuation of DESCOVY.

Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in individuals with HBV who discontinue DESCOVY. If appropriate, anti-hepatitis B therapy may be warranted *[see Warnings and Precautions (5.1)]*.

DESCOVY used for HIV-1 PrEP must only be prescribed to individuals confirmed to be HIV-negative immediately prior to initiating and at least every 3 months during use. Drug-resistant HIV-1 variants have been identified with use of FTC/TDF for HIV-1 PrEP following undetected acute HIV-1 infection. Do not initiate DESCOVY for HIV-1 PrEP if signs or symptoms of acute HIV-1 infection are present unless negative infection status is confirmed *[see Warnings and Precautions (5.2)].*

1 INDICATIONS AND USAGE

1.1 Treatment of HIV-1 Infection

DESCOVY is indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and adolescent patients weighing at least 35 kg.

DESCOVY is indicated for the treatment of HIV-1 infection in pediatric patients weighing at least 14 kg to less than 35 kg in combination with other antiretroviral agents, including darunavir and cobicistat but not other protease inhibitors that require a CYP3A inhibitor.

1.2 HIV-1 Pre-Exposure Prophylaxis (PrEP)

DESCOVY is indicated in at-risk adults and adolescents weighing at least 35 kg for pre-exposure prophylaxis (PrEP) to reduce the risk of HIV-1 infection from sexual acquisition, excluding individuals at risk from receptive vaginal sex. Individuals must have a negative HIV-1 test immediately prior to initiating DESCOVY for HIV-1 PrEP *[see Dosage and Administration (2.2) and Warnings and Precautions (5.2)].*

Limitations of Use:

The indication does not include use of DESCOVY in individuals at risk of HIV-1 from receptive vaginal sex because effectiveness in this population has not been evaluated *[see Clinical Studies (14.3)].*

2 DOSAGE AND ADMINISTRATION

2.1 Testing When Initiating and During Use of DESCOVY for Treatment of HIV-1 Infection or for HIV-1 PrEP

Prior to or when initiating DESCOVY, test individuals for hepatitis B virus infection *[see Warnings and Precautions (5.1)]*.

Prior to or when initiating DESCOVY, and during use of DESCOVY on a clinically appropriate schedule, assess serum creatinine, estimated creatinine clearance, urine glucose, and urine protein in all individuals. In individuals with chronic kidney disease, also assess serum phosphorus *[see Warnings and Precautions (5.4)].*

2.2 HIV-1 Screening for Individuals Receiving DESCOVY for HIV-1 PrEP

Screen all individuals for HIV-1 infection immediately prior to initiating DESCOVY for HIV-1 PrEP and at least once every 3 months while taking DESCOVY, and upon diagnosis of any other sexually transmitted infections (STIs) *[see Indications and Usage (1.2), Contraindications (4), and Warnings and Precautions (5.2)].*

If recent (<1 month) exposures to HIV-1 are suspected or clinical symptoms consistent with acute HIV-1 infection are present, use a test approved or cleared by the FDA as an aid in the diagnosis of acute or primary HIV-1 infection *[see Warnings and Precautions (5.2), Use in Specific Populations (8.4), and Clinical Studies (14.3)].*

2.3 Recommended Dosage for Treatment of HIV-1 Infection in Adults and Pediatric Patients Weighing at Least 35 kg

DESCOVY is a two-drug fixed dose combination product containing emtricitabine (FTC) and tenofovir alafenamide (TAF).

The recommended dosage of DESCOVY for treatment of HIV-1 is one tablet containing 200 mg FTC and 25 mg of TAF taken orally once daily with or without food in:

- adults and pediatric patients with body weight at least 35 kg and estimated creatinine clearance greater than or equal to 30 mL per minute; or
- adults with creatinine clearance below 15 mL per minute who are receiving chronic hemodialysis. On days of hemodialysis, administer the daily dose of DESCOVY after completion of hemodialysis treatment *[see Use in Specific Populations (8.6) and*

Clinical Pharmacology (12.3)].

The safety and effectiveness of DESCOVY coadministered with an HIV-1 protease inhibitor that is administered with either ritonavir or cobicistat have not been established in adults with creatinine clearance below 15 mL per minute, with or without hemodialysis.

For specific dosing recommendations for coadministered antiretroviral drugs, refer to their respective prescribing information *[see Drug Interactions (7)]*.

2.4 Recommended Dosage for Treatment of HIV-1 Infection in Pediatric Patients Weighing at Least 14 kg to Less than 35 kg

The recommended dosage of DESCOVY for treatment of HIV-1 in pediatric patients is based on body weight and is provided in Table 1. This dosing information is applicable to pediatric patients with estimated creatinine clearance greater than or equal to 30 mL per minute *[see Use in Specific Populations (8.6) and Clinical Pharmacology (12.3)]* who are receiving DESCOVY with other antiretroviral agents, including darunavir (DRV) and cobicistat (COBI) but not including other HIV-1 protease inhibitors that are administered with either ritonavir or cobicistat.

Table 1 Dosing for Treatment of HIV-1 Infection in Pediatric Patients Weighing 14 to Less than 35 kg

Body Weight (kg)	**DESCOVY Dosage**
25 kg to less than 35 kg	One tablet containing 200 mg of FTC and 25 mg of TAF taken orally once daily
14 kg to less than 25 kg	One tablet containing 120 mg of FTC and 15 mg of TAF taken orally once daily

For specific dosing recommendations for coadministered antiretroviral drugs, refer to their respective prescribing information *[see Drug Interactions (7)]*.

2.5 Recommended Dosage for HIV-1 PrEP in Adults and Adolescents Weighing at Least 35 kg

The dosage of DESCOVY for HIV-1 PrEP is one tablet (containing 200 mg of FTC and 25 mg of TAF) once daily taken orally with or without food in:

- adults and adolescents without HIV-1 weighing at least 35 kg and with a creatinine clearance greater than or equal to 30 mL per minute; or
- adults without HIV-1 and with creatinine clearance below 15 mL per minute who are receiving chronic hemodialysis. On days of hemodialysis, administer the daily dose of DESCOVY after completion of hemodialysis treatment *[see Indications and Usage (1.2) and Clinical Pharmacology (12.3)].*

2.6 Not Recommended in Individuals with Severe Renal Impairment for Treatment of HIV-1 Infection or for HIV-1 PrEP

DESCOVY is not recommended in individuals with:

- severe renal impairment (estimated creatinine clearance of 15 to below 30 mL per minute); or

- end stage renal disease (ESRD; estimated creatinine clearance below 15 mL per minute) who are not receiving chronic hemodialysis *[see Dosage and Administration (2.3, 2.5) and Use in Specific Populations (8.6)]*.

3 DOSAGE FORMS AND STRENGTHS

DESCOVY tablets are available in two dose strengths:

- 200 mg/25 mg tablets: 200 mg of emtricitabine (FTC) and 25 mg of tenofovir alafenamide (TAF) (equivalent to 28 mg of tenofovir alafenamide fumarate). These tablets are blue, rectangular-shaped, film-coated, debossed with “GSI” on one side and “225” on the other side.
- 120 mg/15 mg tablets: 120 mg of FTC and 15 mg of TAF (equivalent to 16.8 mg of tenofovir alafenamide fumarate). These tablets are white, round-shaped, film coated, debossed with “GSI” on one side and “15” on the other side.

4 CONTRAINDICATIONS

DESCOVY for HIV-1 PrEP is contraindicated in individuals with unknown or positive HIV-1 status *[see Warnings and Precautions (5.2)].*

5 WARNINGS AND PRECAUTIONS

5.1 Severe Acute Exacerbation of Hepatitis B in Individuals with HBV

All individuals should be tested for the presence of hepatitis B virus (HBV) before or when initiating DESCOVY *[see Dosage and Administration (2.1)]*.

Severe acute exacerbations of hepatitis B (e.g., liver decompensation and liver failure) have been reported in individuals with HBV who have discontinued products containing FTC and/or tenofovir disoproxil fumarate (TDF) and may occur with discontinuation of DESCOVY. Individuals with HBV who discontinue DESCOVY should be closely monitored with both clinical and laboratory follow-up for at least several months after stopping treatment. If appropriate, anti-hepatitis B therapy may be warranted, especially in individuals with advanced liver disease or cirrhosis, since post-treatment exacerbation of hepatitis may lead to hepatic decompensation and liver failure. Individuals without HBV should be offered vaccination.

5.2 Comprehensive Management to Reduce the Risk of Sexually Transmitted Infections, Including HIV-1, and Development of HIV-1 Resistance When DESCOVY Is Used for HIV-1 PrEP

Use DESCOVY for HIV-1 PrEP to reduce the risk of HIV-1 infection as part of a comprehensive prevention strategy, including adherence to daily administration and safer sex practices, including condoms, to reduce the risk of sexually transmitted infections (STIs). The time from initiation of DESCOVY for HIV-1 PrEP to maximal protection against HIV-1 infection is unknown.

Risk for HIV-1 acquisition includes behavioral, biological, or epidemiologic factors including but not limited to condomless sex, past or current STIs, self-identified HIV risk, having sexual partners of unknown HIV-1 viremic status, or sexual activity in a high

prevalence area or network.

Counsel individuals on the use of other prevention measures (e.g., consistent and correct condom use, knowledge of partner(s)' HIV-1 status, including viral suppression status, regular testing for STIs that can facilitate HIV-1 transmission). Inform individuals without HIV-1 about, and support their efforts in, reducing sexual risk behavior.

Use DESCOVY to reduce the risk of acquiring HIV-1 only in individuals confirmed to be HIV-1 negative. HIV-1 resistance substitutions may emerge in individuals with undetected HIV-1 infection who are taking only DESCOVY, because DESCOVY alone does not constitute a complete regimen for HIV-1 treatment *[see Microbiology (12.4)];* therefore, care should be taken to minimize the risk of initiating or continuing DESCOVY before confirming the individual is HIV-1 negative.

- Some HIV-1 tests only detect anti-HIV antibodies and may not identify HIV-1 during the acute stage of infection. Prior to initiating DESCOVY for HIV-1 PrEP, ask seronegative individuals about recent (in past month) potential exposure events (e.g., condomless sex or condom breaking during sex with a partner of unknown HIV-1 status or unknown viremic status, or a recent STI), and evaluate for current or recent signs or symptoms consistent with acute HIV-1 infection (e.g., fever, fatigue, myalgia, skin rash).
- If recent (<1 month) exposures to HIV-1 are suspected or clinical symptoms consistent with acute HIV-1 infection are present, use a test approved or cleared by the FDA as an aid in the diagnosis of acute or primary HIV-1 infection.

While using DESCOVY for HIV-1 PrEP, HIV-1 testing should be repeated at least every 3 months, and upon diagnosis of any other STIs.

- If an HIV-1 test indicates possible HIV-1 infection, or if symptoms consistent with acute HIV-1 infection develop following a potential exposure event, convert the HIV-1 PrEP regimen to an HIV treatment regimen until negative infection status is confirmed using a test approved or cleared by the FDA as an aid in the diagnosis of acute or primary HIV-1 infection.

Counsel individuals without HIV-1 to strictly adhere to the once daily DESCOVY dosing schedule. The effectiveness of DESCOVY in reducing the risk of acquiring HIV-1 is strongly correlated with adherence, as demonstrated by measurable drug levels in a clinical trial of DESCOVY for HIV-1 PrEP. Some individuals, such as adolescents, may benefit from more frequent visits and counseling to support adherence *[see Use in Specific Populations (8.4), Microbiology (12.4), and Clinical Studies (14.3)].*

5.3 Immune Reconstitution Syndrome

Immune reconstitution syndrome has been reported in patients with HIV-1 treated with combination antiretroviral therapy, including FTC, a component of DESCOVY. During the initial phase of combination antiretroviral treatment, patients with HIV-1 whose immune system responds may develop an inflammatory response to indolent or residual opportunistic infections (such as *Mycobacterium avium* infection, cytomegalovirus, *Pneumocystis jirovecii* pneumonia [PCP], or tuberculosis), which may necessitate further evaluation and treatment.

Autoimmune disorders (such as Graves' disease, polymyositis, Guillain-Barré syndrome, and autoimmune hepatitis) have also been reported to occur in the setting of immune reconstitution; however, the time to onset is more variable, and can occur many months

after initiation of treatment.

5.4 New Onset or Worsening Renal Impairment

Postmarketing cases of renal impairment, including acute renal failure, proximal renal tubulopathy (PRT), and Fanconi syndrome have been reported with TAF-containing products; while most of these cases were characterized by potential confounders that may have contributed to the reported renal events, it is also possible these factors may have predisposed patients to tenofovir-related adverse events *[see Adverse Reactions (6.1, 6.2)]*. DESCOVY is not recommended in individuals with estimated creatinine clearance of 15 to below 30 mL per minute, or in individuals with estimated creatinine clearance below 15 mL per minute who are not receiving chronic hemodialysis.

Individuals taking tenofovir prodrugs who have impaired renal function and those taking nephrotoxic agents including non-steroidal anti-inflammatory drugs are at increased risk of developing renal-related adverse reactions.

Prior to or when initiating DESCOVY, and during treatment with DESCOVY on a clinically appropriate schedule, assess serum creatinine, estimated creatinine clearance, urine glucose, and urine protein in all individuals. In individuals with chronic kidney disease, also assess serum phosphorus. Discontinue DESCOVY in individuals who develop clinically significant decreases in renal function or evidence of Fanconi syndrome.

5.5 Lactic Acidosis/Severe Hepatomegaly with Steatosis

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including emtricitabine, a component of DESCOVY, and tenofovir DF, another prodrug of tenofovir, alone or in combination with other antiretrovirals. Treatment with DESCOVY should be suspended in any individual who develops clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity (which may include hepatomegaly and steatosis even in the absence of marked transaminase elevations).

6 ADVERSE REACTIONS

The following adverse reactions are discussed in other sections of the labeling:

- Severe Acute Exacerbations of Hepatitis B *[see Warnings and Precautions (5.1)]*.
- Immune Reconstitution Syndrome *[see Warnings and Precautions (5.3)]*.
- New Onset or Worsening Renal Impairment *[see Warnings and Precautions (5.4)]*.
- Lactic Acidosis/Severe Hepatomegaly with Steatosis *[see Warnings and Precautions (5.5)].*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug (or a drug given in various combinations with other concomitant therapy) cannot be directly compared to rates in the clinical trials of another drug (or drug given in the same or different combination therapy) and may not reflect the rates observed in practice.

Adverse Reactions in Clinical Trials of FTC+TAF with Elvitegravir (EVG) plus Cobicistat (COBI) in Treatment-Naïve Adults with HIV-1

In pooled 48-week trials of antiretroviral treatment-naïve adult participants with HIV-1, the most common adverse reaction in participants treated with FTC+TAF with EVG+COBI (N=866) (incidence greater than or equal to 10%, all grades) was nausea (10%). In this treatment group, 0.9% of participants discontinued FTC+TAF with EVG+COBI due to adverse events during the 48-week treatment period *[see Clinical Studies (14.2)]*. The safety profile was similar in virologically-suppressed adults with HIV-1 who were switched to FTC+TAF with EVG+COBI (N=799). Antiretroviral treatment-naïve adult participants with HIV-1 treated with FTC+TAF with EVG+COBI experienced mean increases of 30 mg/dL of total cholesterol, 15 mg/dL of LDL cholesterol, 7 mg/dL of HDL cholesterol, and 29 mg/dL of triglycerides after 48 weeks of use.

Renal Laboratory Tests

In two 48-week trials in antiretroviral treatment-naïve adults with HIV-1 treated with FTC+TAF with EVG+COBI (N=866) with a median baseline eGFR of 115 mL per minute, mean serum creatinine increased by 0.1 mg per dL from baseline to Week 48. Median urine protein-to-creatinine ratio (UPCR) was 44 mg per gram at baseline and at Week 48. In a 48-week trial in virologically-suppressed TDF-treated adults with HIV-1 who switched to FTC+TAF with EVG+COBI (N=959) with a mean baseline eGFR of 112 mL per minute, mean serum creatinine was similar to baseline at Week 48; median UPCR was 61 mg per gram at baseline and 46 mg per gram at Week 48. Across these trials, renal serious adverse events or discontinuations due to renal adverse reactions were encountered in less than 1% of participants treated with FTC+TAF with EVG+COBI.

In a 24-week trial in adults with HIV-1 and renal impairment (baseline eGFR 30 to 69 mL per minute) who received FTC+TAF with EVG+COBI (N=248), mean serum creatinine was 1.5 mg per dL at both baseline and Week 24. Median UPCR was 161 mg per gram at baseline and 93 mg per gram at Week 24. FTC+TAF with EVG+COBI was permanently discontinued due to worsening renal function in two of 80 (3%) participants.

Bone Mineral Density Effects

In the pooled analysis of two 48-week trials of antiretroviral treatment-naïve adult participants with HIV-1, bone mineral density (BMD) from baseline to Week 48 was assessed by dual-energy X-ray absorptiometry (DXA). Mean BMD decreased from baseline to Week 48 −1.30% with FTC+TAF with EVG+COBI at the lumbar spine and −0.66% at the total hip. BMD declines of 5% or greater at the lumbar spine were experienced by 10% of FTC+TAF with EVG+COBI participants. BMD declines of 7% or greater at the femoral neck were experienced by 7% of FTC+TAF with EVG+COBI participants. The long-term clinical significance of these BMD changes is not known.

In 799 virologically-suppressed TDF-treated adult participants with HIV-1 that switched to FTC+TAF with EVG+COBI, at Week 48 mean BMD increased (1.86% lumbar spine, 1.95% total hip). BMD declines of 5% or greater at the lumbar spine were experienced by 1% of FTC+TAF with EVG+COBI participants. BMD declines of 7% or greater at the femoral neck were experienced by 1% of FTC+TAF with EVG+COBI participants.

<u>Adverse Reactions in a Clinical Trial of FTC+TAF with EVG+COBI in Virologically-Suppressed Adults with HIV-1 and End Stage Renal Disease (ESRD) Receiving Chronic Hemodialysis</u>

In a 48-week trial of virologically-suppressed adult participants with HIV-1 and end stage renal disease (ESRD) (estimated creatinine clearance of less than 15 mL/min) on chronic hemodialysis treated with FTC+TAF with EVG+COBI (N=55), the most commonly

reported adverse reaction (adverse event assessed as causally related by investigator and all grades) was nausea (7%). Serious adverse events were reported in 53% of participants and the most common serious adverse events were pneumonia (13%), fluid overload (7%), hyperkalemia (7%) and osteomyelitis (7%). Overall 5% of participants permanently discontinued treatment due to an adverse event.

Adverse Reactions in Clinical Trials in Pediatric Participants with HIV-1

Study 106: Adverse Reactions in a Clinical Trial of FTC+TAF with EVG+COBI in Pediatric Participants Weighing at Least 25 kg

The safety profile of FTC+TAF in pediatric participants weighing at least 25 kg is informed by an open-label trial of antiretroviral treatment-naïve pediatric participants with HIV-1 between the ages of 12 to less than 18 years weighing at least 35 kg through 48 weeks (N=50; cohort 1) and virologically-suppressed participants with HIV-1 between the ages of 6 to less than 12 years weighing at least 25 kg (N=52; cohort 2). Participants received FTC+TAF with EVG+COBI through 48 weeks. With the exception of a decrease in the mean CD4+ cell count observed in cohort 2, the safety of this combination was similar to that in adults.

Bone Mineral Density Effects

Cohort 1: Treatment-naïve adolescents (12 to less than 18 years; at least 35 kg)

Among the participants in cohort 1 receiving FTC+TAF with EVG+COBI, mean BMD increased from baseline to Week 48, +4.2% at the lumbar spine and +1.3% for the total body less head (TBLH). Mean changes from baseline BMD Z-scores were −0.07 for lumbar spine and −0.20 for TBLH at Week 48. One participant had significant (at least 4%) lumbar spine BMD loss at Week 48.

Cohort 2: Virologically-suppressed children (6 to less than 12 years; at least 25 kg)

Among the participants in cohort 2 receiving FTC+TAF with EVG+COBI, mean BMD increased from baseline to Week 48, +3.9% at the lumbar spine and +4.2% for TBLH. Mean changes from baseline BMD Z-scores were -0.24 for lumbar spine and -0.19 for TBLH at Week 48. Six participants had significant (at least 4%) lumbar spine BMD loss at Week 48 and 2 participants also had at least 4% TBLH BMD loss at Week 48.

Change from Baseline in CD4+ cell counts

Cohort 2: Virologically-suppressed children (6 to less than 12 years; at least 25 kg)

Cohort 2 evaluated pediatric participants (N=52) who were virologically-suppressed and who switched from their antiretroviral regimen to FTC+TAF with EVG+COBI. Although all participants had HIV-1 RNA < 50 copies/mL, there was a decrease from baseline in CD4+ cell count at Weeks 24 and 48. The mean baseline and mean change from baseline in CD4+ cell count and in CD4% from Week 2 to Week 48 are presented in Table 2. All participants maintained their CD4+ cell counts above 400 cells/mm^3 *[see Use in Specific Populations (8.4)].*

Table 2 Mean Change in CD4+ Count and CD4 Percentage from Baseline to Week 48 in Virologically-Suppressed Pediatric Participants from 6 to <12 Years Who Switched to FTC+TAF with EVG+COBI

	Baseline	Mean Change from Baseline					
		Week 2	Week 4	Week 12	Week 24	Week 32	Week 48
CD4+ Cell Count (cells/mm^3)	961 (275.5)*	-117	-114	-112	-118	-62	-66
CD4%	38 (6.4)*	+0.3%	-0.1%	-0.8%	-0.8%	-1.0%	-0.6%

* Mean (SD)

Study 1474: Adverse Reactions in a Clinical Trial of FTC+TAF with Bictegravir in Pediatric Participants Weighing at Least 14 to Less Than 25 kg

In a separate open-label trial of virologically-suppressed participants at least 2 years of age and weighing at least 14 to less than 25 kg (N=22; cohort 3) who received FTC+TAF with bictegravir through 24 weeks, no new adverse reactions or laboratory abnormalities were identified compared to those observed in adults. In this trial, the mean (SD) change from baseline to Week 24 in CD4+ cell count was −126 (264) cells per mm^3 and the mean (SD) change in CD4% from baseline to Week 24 was 0.2% (4.4%).

Study 128: Adverse Reactions in a Clinical Trial of DESCOVY in combination with Darunavir+Cobicistat (DRV+COBI) in Pediatric Participants Weighing at Least 14 kg

The safety profile of DESCOVY is also informed by a separate open-label trial of virologically-suppressed pediatric participants between the ages of 6 to less than 12 years and weighing at least 25 to less than 40 kg (N=9; cohort 2), and virologically-suppressed pediatric participants at least 2 years of age and weighing at least 14 to less than 25 kg (N=11; cohort 3) who received DESCOVY in combination with DRV+COBI through Week 48. In this study, the safety profile of DESCOVY was similar to that in adults.

Bone Mineral Density Effects

Cohort 2: Pediatric Participants Weighing at Least 25 to Less Than 40 kg

Among the participants in cohort 2 who had both baseline and Week 48 measurements (n=8 and 9 for lumbar spine and TBLH, respectively), mean BMD increased from baseline to Week 48, +6.1% at lumbar spine and +4.4% for TBLH.

Cohort 3: Pediatric Participants Weighing at Least 15 to less Than 25 kg

Among the participants in cohort 3 who had both baseline and Week 48 measurements (n=7 and 10 for lumbar spine and TBLH, respectively), mean BMD increased from baseline to Week 48, +8.7% at lumbar spine and +6.9% for TBLH.

Adverse Reactions from Clinical Trial Experience in Individuals without HIV-1 Taking DESCOVY for HIV-1 PrEP

The safety profile of DESCOVY for HIV-1 PrEP was comparable to that observed in clinical trials of participants with HIV based on a double-blind, randomized, active-controlled trial (DISCOVER) in which a total of 5,387 adult men and transgender women without HIV-1 who have sex with men received DESCOVY (N=2,694) or TRUVADA (N=2,693) once daily for HIV-1 PrEP *[see Clinical Studies (14.3)]*. Median duration of exposure was 86 and 87 weeks, respectively. The most common adverse reaction in

participants who received DESCOVY (incidence greater than or equal to 5%, all grades) was diarrhea (5%). Table 3 provides a list of the most common adverse reactions that occurred in 2% or more of participants in either treatment group. The proportion of participants who discontinued treatment with DESCOVY or TRUVADA due to adverse events, regardless of severity, was 1.3% and 1.8%, respectively.

Table 3 Adverse Reactions (All Grades) Reported in ≥2% in Either Arm in the DISCOVER Trial of Participants without HIV-1

	DESCOVY (N=2,694)	TRUVADA (N=2,693)
Diarrhea	5%	6%
Nausea	4%	5%
Headache	2%	2%
Fatigue	2%	3%
Abdominal pain*	2%	3%

* Includes the following terms: abdominal pain, abdominal pain upper, abdominal pain lower, gastrointestinal pain, and abdominal discomfort

Renal Laboratory Tests

Changes from baseline to Week 48 in renal laboratory data are presented in Table 4. The long-term clinical significance of these renal laboratory changes on adverse reaction frequencies between DESCOVY and TRUVADA is not known.

Table 4 Laboratory Assessments of Renal Function Reported in Participants without HIV-1 Receiving DESCOVY or TRUVADA in the DISCOVER Trial

	DESCOVY (N=2,694)	TRUVADA (N=2,693)
Serum Creatinine (mg/dL)*		
Change at Week 48	−0.01 (0.107)	0.01 (0.111)
$eGFR_{CG}$ (mL/min)†		
Change at Week 48	1.8 (−7.2, 11.1)	−2.3 (−10.8, 7.2)
Percentage of Participants who Developed UPCR >200 mg/g‡		
At Week 48	0.7%	1.5%

$eGFR_{CG}$=estimated Glomerular Filtration Rate by Cockcroft-Gault; UPCR=urine protein/creatinine ratio

* Mean (SD).
† Median (Q1, Q3).
‡ Based on N who had normal UPCR (≤ 200 mg/g) at baseline.

Bone Mineral Density Effects

In the DISCOVER trial, mean increases from baseline to Week 48 of 0.5% at the lumbar spine (N=159) and 0.2% at the total hip (N=158) were observed in participants receiving DESCOVY, compared to mean decreases of 1.1% at the lumbar spine (N=160) and 1.0% at the total hip (N=158) in participants receiving TRUVADA. BMD declines of 5% or greater at the lumbar spine and 7% or greater at the total hip were experienced by 4% and 1% of participants, respectively, in both treatment groups at Week 48. The long-term clinical significance of these BMD changes is not known.

Serum Lipids

Changes from baseline to Week 48 in total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides, and total cholesterol to HDL ratio are presented in Table 5.

Table 5 Fasting Lipid Values, Mean Change from Baseline, Reported in Participants without HIV-1 Receiving DESCOVY or TRUVADA in the DISCOVER Trial*

	DESCOVY (N=2,694)		TRUVADA (N=2,693)	
	Baseline	Week 48	Baseline	Week 48
	mg/dL	Change†	mg/dL	Change†
Total Cholesterol (fasted)	176 ‡	0 ‡	176 §	-12 §
HDL-Cholesterol (fasted)	51 ‡	-2 ‡	51 §	-5 §
LDL-Cholesterol (fasted)	103 ¶	0 ¶	103 #	-7 #
Triglycerides (fasted)	109 ‡	+9 ‡	111 §	-1 §
Total Cholesterol to HDL ratio	3.7 ‡	0.2 ‡	3.7 §	0.1 §

* Excludes participants who received lipid lowering agents during the treatment period.
† The baseline and change from baseline are for participants with both baseline and Week 48 values.
‡ N=1,098
§ N=1,124
¶ N=1,079
# N=1,107

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of products containing TAF. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Skin and Subcutaneous Tissue Disorders
Angioedema, urticaria, and rash

Renal and Urinary Disorders

Acute renal failure, acute tubular necrosis, proximal renal tubulopathy, and Fanconi syndrome

7 DRUG INTERACTIONS

7.1 Potential for Other Drugs to Affect One or More Components of DESCOVY

TAF, a component of DESCOVY, is a substrate of P-gp, BCRP, OATP1B1, and OATP1B3. Drugs that strongly affect P-gp and BCRP activity may lead to changes in TAF absorption (see Table 6). Drugs that induce P-gp activity are expected to decrease the absorption of TAF, resulting in decreased plasma concentration of TAF, which may lead to loss of therapeutic effect of DESCOVY and development of resistance. Coadministration of DESCOVY with other drugs that inhibit P-gp and BCRP may increase the absorption and plasma concentration of TAF. TAF is not an inhibitor of CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, or UGT1A1. TAF is a weak inhibitor of CYP3A *in vitro*. TAF is not an inhibitor or inducer of CYP3A *in vivo*.

7.2 Drugs Affecting Renal Function

Because FTC and tenofovir are primarily excreted by the kidneys by a combination of glomerular filtration and active tubular secretion, coadministration of DESCOVY with drugs that reduce renal function or compete for active tubular secretion may increase concentrations of FTC, tenofovir, and other renally eliminated drugs and this may increase the risk of adverse reactions. Some examples of drugs that are eliminated by active tubular secretion include, but are not limited to, acyclovir, cidofovir, ganciclovir, valacyclovir, valganciclovir, aminoglycosides (e.g., gentamicin), and high-dose or multiple NSAIDs *[see Warnings and Precautions (5.4)]*.

7.3 Established and Other Potentially Significant Interactions

Table 6 provides a listing of established or potentially clinically significant drug interactions with recommended steps to prevent or manage the drug interaction (the table is not all inclusive). The drug interactions described are based on studies conducted with either DESCOVY, the components of DESCOVY (emtricitabine and tenofovir alafenamide) as individual agents, or are predicted drug interactions that may occur with DESCOVY. For magnitude of interaction, *see Clinical Pharmacology (12.3)*.

Table 6 Established and Other Potentially Significant* Drug Interactions

Concomitant Drug Class: Drug Name	Effect on Concentration†	Clinical Comment
Antiretroviral Agents: Protease Inhibitors (PI)		
tipranavir/ritonavir	↓ TAF	Coadministration with DESCOVY is not recommended.
		Coadministration with DESCOVY in pediatric patients weighing 14 to <

atazanavir/cobicistat	↑ TAF	35 kg is not recommended *[see Use in Specific Populations (8.4)]*.
Other Agents		
Anticonvulsants: carbamazepine oxcarbazepine phenobarbital phenytoin	↓ TAF	Consider alternative anticonvulsant.
Antimycobacterials: rifabutin rifampin rifapentine	↓ TAF	Coadministration of DESCOVY with rifabutin, rifampin, or rifapentine is not recommended.
Herbal Products: St. John's wort *(Hypericum perforatum)*	↓ TAF	Coadministration of DESCOVY with St. John's wort is not recommended.

↑= Increase
∗ This table is not all inclusive.
† ↓=Decrease

7.4 Drugs without Clinically Significant Interactions with DESCOVY

Based on drug interaction studies conducted with the components of DESCOVY, no clinically significant drug interactions have been either observed or are expected when DESCOVY is combined with the following antiretroviral agents: atazanavir with ritonavir, atazanavir with cobicistat (in those weighing ≥35 kg), darunavir with ritonavir or cobicistat, dolutegravir, efavirenz, ledipasvir, lopinavir/ritonavir, maraviroc, nevirapine, raltegravir, rilpivirine, and sofosbuvir.

No clinically significant drug interactions have been either observed or are expected when DESCOVY is combined with the following drugs: buprenorphine, itraconazole, ketoconazole, lorazepam, methadone, midazolam, naloxone, norbuprenorphine, norgestimate/ethinyl estradiol, and sertraline.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in individuals exposed to DESCOVY during pregnancy. Healthcare providers are encouraged to register individuals by calling the Antiretroviral Pregnancy Registry (APR) at 1-800-258-4263.

Risk Summary

Available data from the APR show no statistically significant difference in the overall risk of major birth defects for emtricitabine (FTC) or tenofovir alafenamide (TAF) compared

with the background rate for major birth defects of 2.7% in a U.S. reference population of the Metropolitan Atlanta Congenital Defects Program (MACDP) *(see Data)*. The rate of miscarriage for individual drugs is not reported in the APR. The estimated background rate of miscarriage in the clinically recognized pregnancies in the U.S. general population is 15–20%.

In animal studies, no adverse developmental effects were observed when the components of DESCOVY were administered separately during the period of organogenesis at exposures 60 and 108 times (mice and rabbits, respectively) the FTC exposure and at exposure equal to or 53 times (rats and rabbits, respectively) the TAF exposure at the recommended daily dose of DESCOVY *(see Data).* Likewise, no adverse developmental effects were seen when FTC was administered to mice through lactation at exposures up to approximately 60 times the exposure at the recommended daily dose of DESCOVY. No adverse effects were observed in the offspring when TDF was administered through lactation at tenofovir exposures of approximately 14 times the exposure at the recommended daily dosage of DESCOVY.

Data

Human Data

Prospective reports from the APR of overall major birth defects in pregnancies exposed to the components of DESCOVY are compared with a U.S. background major birth defect rate. Methodological limitations of the APR include the use of MACDP as the external comparator group. The MACDP population is not disease-specific, evaluates women and infants from a limited geographic area, and does not include outcomes for births that occurred at less than 20 weeks gestation.

Emtricitabine (FTC):

Based on prospective reports to the APR of over 7300 exposures to FTC-containing regimens during pregnancy resulting in live births (including over 5400 exposed in the first trimester and over 1800 exposed in the second/third trimester), the prevalence of birth defects in live births was 3.0% (95% CI: 2.5% to 3.5%) and 2.7% (95% CI: 2.0% to 3.6%) following first and second/third trimester exposure, respectively, to FTC-containing regimens.

Tenofovir Alafenamide (TAF):

Based on prospective reports to the APR of over 1600 exposures to TAF-containing regimens during pregnancy resulting in live births (including over 1300 exposed in the first trimester and over 300 exposed in the second/third trimester), the prevalence of birth defects in live births was 3.9% (95% CI: 2.9% to 5.2%) and 4.7% (95% CI: 2.6% to 7.7%) following first and second/third trimester exposure, respectively, to TAF-containing regimens.

Animal Data

Emtricitabine: FTC was administered orally to pregnant mice (250, 500, or 1000 mg/kg/day) and rabbits (100, 300, or 1000 mg/kg/day) through organogenesis (on gestation days 6 through 15, and 7 through 19, respectively). No significant toxicological effects were observed in embryo-fetal toxicity studies performed with FTC in mice at exposures (area under the curve [AUC]) approximately 60 times higher and in rabbits at approximately 108 times higher than human exposures at the recommended daily dose. In a pre/postnatal development study with FTC, mice were administered

doses up to 1000 mg/kg/day; no significant adverse effects directly related to drug were observed in the offspring exposed daily from before birth (*in utero*) through sexual maturity at daily exposures (AUC) of approximately 60-fold higher than human exposures at the recommended daily dose.

Tenofovir Alafenamide: TAF was administered orally to pregnant rats (25, 100, or 250 mg/kg/day) and rabbits (10, 30, or 100 mg/kg/day) through organogenesis (on gestation days 6 through 17, and 7 through 20, respectively). No adverse embryo-fetal effects were observed in rats and rabbits at TAF exposures approximately similar to (rats) and 53 (rabbits) times higher than the exposure in humans at the recommended daily dose of DESCOVY. TAF is rapidly converted to tenofovir; the observed tenofovir exposures in rats and rabbits were 59 (rats) and 93 (rabbits) times higher than human tenofovir exposures at the recommended daily dose. Since TAF is rapidly converted to tenofovir and a lower tenofovir exposure in rats and mice was observed after TAF administration compared to tenofovir disoproxil fumarate (TDF, another prodrug for tenofovir) administration, a pre/postnatal development study in rats was conducted only with TDF. Doses up to 600 mg/kg/day were administered through lactation; no adverse effects were observed in the offspring on gestation day 7 (and lactation day 20) at tenofovir exposures of approximately 14 (21) times higher than the exposures in humans at the recommended daily dose of DESCOVY.

8.2 Lactation

Risk Summary

Data from the published literature report the presence of FTC, TAF, and tenofovir in human milk. Data from the published literature have not reported adverse effects of FTC or TAF on a breastfed child. There are no data on the effects of FTC or TAF on milk production.

Potential risks of breastfeeding include: 1) HIV transmission to infants without HIV-1; 2) developing viral resistance in infants with HIV-1; and 3) adverse reactions in a breastfed infant similar to those seen in adults.

8.4 Pediatric Use

The safety and effectiveness of DESCOVY for the treatment of HIV-1 infection have been established in pediatric patients weighing at least 14 kg *[see Indications and Usage (1.1) and Dosage and Administration (2.2)]*.

Treatment of HIV-1 Infection

Adolescent Patients Weighing at Least 35 kg:

The safety and effectiveness of DESCOVY in combination with other antiretroviral agents for the treatment of HIV-1 infection was established in adolescent patients weighing at least 35 kg.

Use of DESCOVY in adolescent patients is supported by adequate and well controlled trials of FTC+TAF with EVG+COBI in adults and by an open-label trial in antiretroviral treatment-naïve pediatric participants with HIV-1 aged 12 to less than 18 years and weighing at least 35 kg through Week 48 (N=50; Study 106 [cohort 1]) administered FTC+TAF with EVG+COBI. The safety and effectiveness of FTC+TAF with EVG+COBI in adolescent participants was similar to that in adults on this regimen *[see Adverse*

Reactions (6.1), Clinical Pharmacology (12.3), and Clinical Studies (14.2)].

Pediatric Patients Weighing at least 14 kg and Less than 35 kg:

The safety and effectiveness of DESCOVY in combination with other antiretroviral agents, including darunavir and cobicistat (DRV+COBI) but not including other protease inhibitors that require a CYP3A inhibitor, for the treatment of HIV-1 infection was established in pediatric patients weighing at least 14 kg to less than 35 kg *[see Adverse Reactions (6.1), Clinical Pharmacology (12.3), and Clinical Studies (14.2)]*.

Use of DESCOVY in pediatric patients weighing at least 14 kg to less than 35 kg is supported by:

- adequate and well controlled trials of FTC+TAF with EVG+COBI in adults;
- an open-label trial in virologically-suppressed pediatric participants aged 6 to less than 12 years and weighing at least 25 kg (N=52; Study 106 [cohort 2]) administered FTC+TAF with EVG+COBI through Week 48;
- an open-label trial of DESCOVY administered in combination with DRV+COBI in virologically-suppressed pediatric participants at least 2 years of age and weighing at least 14 kg to less than 40 kg (n=20; Study 128 [cohort 2 and 3]) through Week 48;
- an open-label trial of FTC+TAF with bictegravir in virologically-suppressed pediatric participants at least 2 years of age and weighing at least 14 to less than 25 kg through Week 24 (N=22; Study 1474 [cohort 3]).

  Overall, the safety and effectiveness of FTC+TAF in pediatric participants in these trials were similar to that observed in adults. Specifically, the safety and efficacy of FTC+TAF with EVG+COBI in participants 6 to 12 years of age and weighing at least 25 kg were similar to that in antiretroviral treatment-naïve adults and adolescents receiving this regimen, with the exception of a decrease from baseline in CD4+ cell count. The safety and effectiveness of DESCOVY when administered with DRV+COBI in pediatric participants weighing at least 14 kg to less than 40 kg were similar to that in adults.

Use of DESCOVY with Other Protease Inhibitors that Require CYP3A Inhibition in Pediatric Patients Weighing at least 14 kg to Less than 35 kg:

The use of DESCOVY with atazanavir and cobicistat (ATV+COBI) is not recommended in pediatric patients weighing at least 14 kg to less than 35 kg.

The use of DESCOVY with ATV+COBI was studied in pediatric patients weighing at least 14 kg to less than 35 kg. In Study 128, participants who received ATV+COBI in cohort 2 (25 kg to <40 kg, n=14) and cohort 3 (14 kg to <25 kg, n=15) showed TAF exposures (C_{max} and AUC) that exceeded adult exposures by 4–5-fold in cohort 2, and 2–3-fold in cohort 3. Limited safety data were available to support the increased TAF exposures. Therefore, the use of DESCOVY with ATV+COBI is not recommended in pediatric patients weighing at least 14 kg to less than 35 kg.

Safety and effectiveness of DESCOVY in combination with protease inhibitors that require ritonavir in pediatric patients weighing at least 14 kg to less than 35 kg have not been established.

Pediatric Patients Weighing less than 14 kg:

Safety and effectiveness of DESCOVY for treatment of HIV-1 infection in pediatric patients weighing less than 14 kg have not been established.

HIV-1 PrEP

Safety and effectiveness of DESCOVY for HIV-1 PrEP in at-risk adolescents weighing at least 35 kg, excluding individuals at risk from receptive vaginal sex, is supported by data from an adequate and well-controlled trial of DESCOVY for HIV-1 PrEP in adults with additional data from safety and pharmacokinetic studies in previously conducted trials with the individual drug products, FTC and TAF, with EVG+COBI, in adults and pediatric participants with HIV-1 *[see Dosage and Administration (2.5), Adverse Reactions (6.1), Clinical Pharmacology (12.3 and 12.4), and Clinical Studies (14)].*

While using DESCOVY for HIV-1 PrEP, HIV-1 testing should be repeated at least every 3 months, and upon diagnosis of any other STIs. Previous studies in at-risk adolescents indicated waning adherence to a daily oral PrEP regimen once visits were switched from monthly to quarterly visits. Adolescents may therefore benefit from more frequent visits and counseling *[see Warnings and Precautions (5.2)].*

Safety and effectiveness of DESCOVY for HIV-1 PrEP in pediatric individuals weighing less than 35 kg have not been established.

8.5 Geriatric Use

In clinical trials of an FTC+TAF-containing regimen for treatment of HIV-1, 80 of the 97 participants enrolled aged 65 years and over received FTC+TAF and EVG+COBI. No differences in safety or efficacy have been observed between elderly participants and adults between 18 and less than 65 years of age.

8.6 Renal Impairment

No dosage adjustment of DESCOVY is recommended in individuals with estimated creatinine clearance greater than or equal to 30 mL per minute, or in adults with ESRD (estimated creatinine clearance below 15 mL per minute) who are receiving chronic hemodialysis. On days of hemodialysis, administer the daily dose of DESCOVY after completion of hemodialysis treatment.

Safety and effectiveness of DESCOVY coadministered with an HIV-1 protease inhibitor that is administered with either ritonavir or cobicistat have not been established in patients with ESRD *[see Dosage and Administration (2.3)]*.

DESCOVY is not recommended in individuals with severe renal impairment (estimated creatinine clearance of 15 to below 30 mL per minute), or in individuals with ESRD who are not receiving chronic hemodialysis, as the safety of DESCOVY has not been established in these populations *[see Dosage and Administration (2.6) and Clinical Studies (14.2)].*

8.7 Hepatic Impairment

No dosage adjustment of DESCOVY is recommended in individuals with mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment. DESCOVY has not been studied in individuals with severe hepatic impairment (Child-Pugh Class C) *[see Clinical Pharmacology (12.3)]*.

10 OVERDOSAGE

No data are available on overdose of DESCOVY in patients. If overdose occurs, monitor the individual for evidence of toxicity. Treatment of overdose with DESCOVY consists of general supportive measures including monitoring of vital signs as well as observation of the clinical status of the individual.

Emtricitabine (FTC): Limited clinical experience is available at doses higher than the recommended dose of FTC in DESCOVY. In one clinical pharmacology study, single doses of FTC 1200 mg (6 times the FTC dose in DESCOVY) were administered to 11 participants. No severe adverse reactions were reported. The effects of higher doses are not known.

Hemodialysis treatment removes approximately 30% of the FTC dose over a 3-hour dialysis period starting within 1.5 hours of FTC dosing (blood flow rate of 400 mL per minute and a dialysate flow rate of 600 mL per minute). It is not known whether FTC can be removed by peritoneal dialysis.

Tenofovir Alafenamide (TAF): Limited clinical experience is available at doses higher than the recommended dose of TAF. A single dose of 125 mg TAF (5 times the TAF dose in 200/25 mg DESCOVY) was administered to 48 healthy participants; no serious adverse reactions were reported. The effects of higher doses are unknown. Tenofovir is efficiently removed by hemodialysis with an extraction coefficient of approximately 54%.

11 DESCRIPTION

DESCOVY (emtricitabine and tenofovir alafenamide) is a fixed dose combination tablet containing emtricitabine (FTC) and tenofovir alafenamide (TAF) for oral administration.

- FTC, a synthetic nucleoside analog of cytidine, is an HIV nucleoside analog reverse transcriptase inhibitor (HIV NRTI).
- TAF, an HIV NRTI, is converted in vivo to tenofovir, an acyclic nucleoside phosphonate (nucleotide) analog of adenosine 5′-monophosphate.

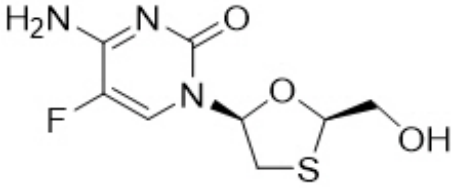
DESCOVY tablets are available in two dose strengths:

- 200 mg/25 mg tablets: 200 mg of FTC and 25 mg of TAF (equivalent to 28 mg of tenofovir alafenamide fumarate).
- 120 mg/15 mg tablets: 120 mg of FTC and 15 mg of TAF (equivalent to 16.8 mg of tenofovir alafenamide fumarate).

Both dose strengths of DESCOVY tablets include the following inactive ingredients: croscarmellose sodium, magnesium stearate, and microcrystalline cellulose. The 200 mg/ 25 mg tablets are film-coated with a coating material containing indigo carmine aluminum lake, polyethylene glycol, polyvinyl alcohol, talc, and titanium dioxide. The 120 mg/15 mg tablets are film-coated with a coating material containing polyvinyl alcohol, titanium dioxide, polyethylene glycol, and talc.

Emtricitabine: The chemical name of FTC is 4-amino-5-fluoro-1-(2*R*-hydroxymethyl-1,3-oxathiolan-5*S*-yl)-(1H)-pyrimidin-2-one. FTC is the (-)enantiomer of a thio analog of cytidine, which differs from other cytidine analogs in that it has a fluorine in the 5 position.

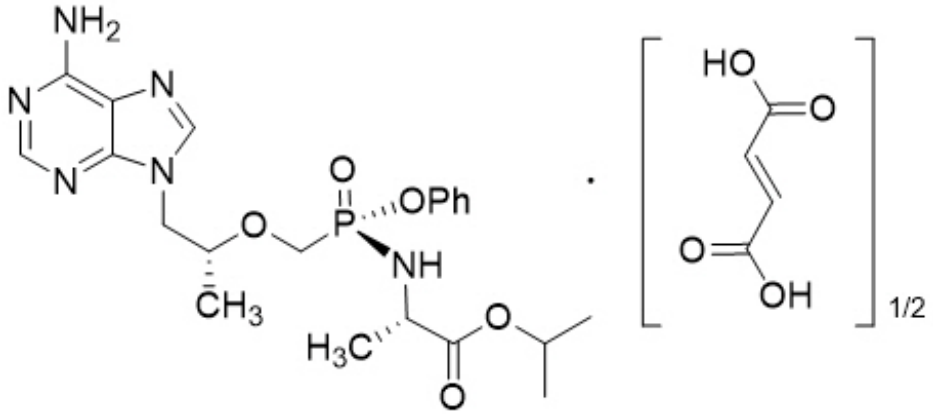
FTC has a molecular formula of $C_8H_{10}FN_3O_3S$ and a molecular weight of 247.24 and has the following structural formula:



FTC is a white to off-white powder with a solubility of approximately 112 mg per mL in water at 25 °C.

Tenofovir Alafenamide: The chemical name of tenofovir alafenamide fumarate drug substance is L-alanine, *N*-[(*S*)-[[(1*R*)-2-(6-amino-9*H*-purin-9-yl)-1-methylethoxy]methyl]phenoxyphosphinyl]-, 1-methylethyl ester, (2*E*)-2-butenedioate (2:1).

Tenofovir alafenamide fumarate has an empirical formula of $C_{21}H_{29}O_5N_6P \bullet ½(C_4H_4O_4)$ and a formula weight of 534.50 and has the following structural formula:



Tenofovir alafenamide fumarate is a white to off-white or tan powder with a solubility of 4.7 mg per mL in water at 20 °C.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

DESCOVY is a fixed dose combination of antiretroviral drugs emtricitabine (FTC) and tenofovir alafenamide (TAF) *[see Microbiology (12.4)]*.

12.2 Pharmacodynamics

Cardiac Electrophysiology

In a thorough QT/QTc study in 48 healthy participants, TAF at the recommended dose or at a dose approximately 5 times the recommended dose, did not affect the QT/QTc interval and did not prolong the PR interval. The effect of the other component of DESCOVY, FTC, or the combination of FTC and TAF on the QT interval is not known.

12.3 Pharmacokinetics

Absorption, Distribution, Metabolism, and Excretion

The pharmacokinetic (PK) properties of the components of DESCOVY are provided in Table 7. The multiple dose PK parameters of FTC and TAF and its metabolite tenofovir are

provided in Table 8. HIV status has no effect on the pharmacokinetics of FTC and TAF in adults.

Table 7 Pharmacokinetic Properties of the Components of DESCOVY

	Emtricitabine	**Tenofovir Alafenamide**
Absorption		
T_{max} (h)	3	1
Effect of high fat meal (relative to fasting)*	AUC Ratio = 0.91 (0.89, 0.93) C_{max} Ratio = 0.74 (0.69, 0.78)	AUC Ratio = 1.75 (1.64, 1.88) C_{max} Ratio= 0.85 (0.75, 0.95)
Distribution		
% Bound to human plasma proteins	<4	~80
Source of protein binding data	*In vitro*	*Ex vivo*
Blood-to-plasma ratio	0.6	1.0
Metabolism		
Metabolism	Not significantly metabolized	Cathepsin A† (PBMCs) CES1 (hepatocytes) CYP3A (minimal)
Elimination		
Major route of elimination	Glomerular filtration and active tubular secretion	Metabolism (>80% of oral dose)
$t_{1/2}$ (h)‡	10	0.51
% Of dose excreted in urine§	70	<1
% Of dose excreted in feces§	13.7	31.7

PBMCs=peripheral blood mononuclear cells;
CES1=carboxylesterase 1

* Values refer to geometric mean ratio [High-fat meal/ fasting] in PK parameters and (90% confidence interval). High-calorie/high-fat meal = ~800 kcal, 50% fat.

† *In vivo*, TAF is hydrolyzed within cells to form tenofovir (major metabolite), which is phosphorylated to the active metabolite, tenofovir diphosphate. *In vitro* studies have shown that TAF is metabolized to tenofovir by cathepsin A in PBMCs and macrophages; and by CES1 in hepatocytes. Upon coadministration with the moderate CYP3A inducer probe efavirenz, TAF exposure was unaffected.

‡ $t_{1/2}$ values refer to median terminal plasma half-life. Note that the pharmacologically active metabolite, tenofovir diphosphate, has a half-life of 150-180 hours within PBMCs.

§ Dosing in mass balance studies: FTC (single dose administration of [^{14}C] emtricitabine after multiple dosing of emtricitabine for 10 days); TAF (single dose administration of [^{14}C] tenofovir alafenamide).

Table 8 Multiple Dose PK Parameters of Emtricitabine, Tenofovir Alafenamide and its Metabolite Tenofovir Following Oral Administration with Food in Adults with HIV-1

Parameter Mean (CV%)	Emtricitabine*	Tenofovir Alafenamide†	Tenofovir‡
C_{max} (microgram per mL)	2.1 (20.2)	0.16 (51.1)	0.02 (26.1)
AUC_{tau} (microgram•hour per mL)	11.7 (16.6)	0.21 (71.8)	0.29 (27.4)
C_{trough} (microgram per mL)	0.10 (46.7)	NA	0.01 (28.5)

CV=Coefficient of Variation; NA=Not Applicable

* From Intensive PK analysis in a phase 2 trial in adults with HIV-1 treated with FTC+TAF and EVG+COBI.

† From Population PK analysis in two trials of treatment-naïve adults with HIV-1 treated with FTC+TAF with EVG+COBI (N=539).

‡ From Population PK analysis in two trials of treatment-naïve adults with HIV-1 treated with FTC+TAF with EVG+COBI (N=841).

Specific Populations

Geriatric Patients

Pharmacokinetics of FTC and TAF have not been fully evaluated in the elderly (65 years of age and older). Population pharmacokinetics analysis of participants with HIV in Phase 2 and Phase 3 trials of FTC+TAF and EVG+COBI showed that age did not have a clinically relevant effect on exposures of TAF up to 75 years of age *[see Use in Specific Populations (8.5)]*.

Pediatric Patients

Treatment of HIV-1 Infection: Mean exposures of TAF in 24 pediatric participants with HIV-1 aged 12 to less than 18 years who received FTC+TAF with EVG+COBI were decreased (23% for AUC) and FTC exposures were similar compared to exposures achieved in treatment-naïve adults following administration of this dosage regimen. The TAF exposure differences are not thought to be clinically significant based on exposure-response relationships (Table 9).

Table 9 Multiple Dose PK Parameters of Emtricitabine, Tenofovir Alafenamide, and its Metabolite Tenofovir Following Oral Administration of FTC+TAF with EVG+COBI in Pediatric Participants with HIV-1 Aged 12 to less than 18 Years*

Parameter Mean (CV%)	Emtricitabine	Tenofovir Alafenamide	Tenofovir

C_{max} (microgram per mL)	2.3 (22.5)	0.17 (64.4)	0.02 (23.7)
AUC_{tau} (microgram•hour per mL)	14.4 (23.9)	0.20† (50.0)	0.29† (18.8)
C_{trough} (microgram per mL)	0.10† (38.9)	NA	0.01 (21.4)

CV = Coefficient of Variation; NA = Not Applicable

* From Intensive PK analysis in a trial in treatment-naïve pediatric participants with HIV-1 infection (N=24).

† N=23

Exposures of FTC and TAF achieved in 23 pediatric participants with HIV-1 between the ages of 6 to less than 12 years and weighing at least 25 kg (55 lbs) who received FTC+TAF with EVG+COBI were higher (20% to 80% for AUC) than exposures achieved in adults receiving this same dosage regimen; the increases were not considered clinically significant (Table 10) *[see Use in Specific Populations (8.4)]*.

Table 10 Multiple Dose PK Parameters of Emtricitabine, Tenofovir Alafenamide and its Metabolite Tenofovir Following Oral Administration of FTC+TAF with EVG+COBI in Pediatric Participants with HIV-1 Aged 6 to less than 12 Years*

Parameter Mean (CV%)	Emtricitabine	Tenofovir Alafenamide	Tenofovir
C_{max} (microgram per mL)	3.4 (27.0)	0.31 (61.2)	0.03 (20.8)
AUC_{tau} (microgram•hour per mL)	20.6† (18.9)	0.33 (44.8)	0.44 (20.9)
C_{trough} (microgram per mL)	0.11 (24.1)	NA	0.02 (24.9)

CV = Coefficient of Variation; NA = Not Applicable

* From Intensive PK analysis in a trial in virologically-suppressed pediatric participants with HIV-1 (N=23).

† N=22

Exposures of FTC and TAF (AUC_{tau} and C_{max}) achieved in 22 pediatric participants with HIV-1 at least 2 years of age and weighing from 14 to less than 25 kg who received FTC+TAF with bictegravir were higher than exposures in adults; the increases were not considered clinically significant as the safety profiles were similar in adult and pediatric patients (Table 11) *[see Use in Specific Populations (8.4)]*.

Table 11 Multiple Dose Pharmacokinetic Parameters

of Emtricitabine and Tenofovir Alafenamide Following Oral Administration of FTC+TAF with Bictegravir in Pediatric Participants with HIV-1 at least 2 Years of Age and Weighing from 14 to Less than 25 kg*

Parameter Mean (CV%)	Emtricitabine†	Tenofovir Alafenamide†
C_{max} (microgram per mL)	3.85 (34.7)	0.414 (31.0)
AUC_{tau} (microgram•h per mL)	15.0 (21.9)	0.305 (42.6)
C_{trough} (microgram per mL)	0.210 (243)	NA

CV = Coefficient of Variation; NA = Not Applicable

* This trial enrolled virologically-suppressed pediatric participants with HIV-1 from 3 to 9 years of age.

† From Intensive PK analysis (n=12 except n=11 for C_{trough} for FTC).

Exposures of FTC and TAF (AUC_{tau} and C_{max}) achieved in 9 pediatric participants with HIV-1 between the ages of 6 to less than 12 years and weighing at least 25 kg to less than 40 kg who received DESCOVY in combination with DRV+COBI were generally higher than exposures achieved in adults; however, the increases were not considered clinically significant (Table 12).

Table 12 Multiple Dose Pharmacokinetic Parameters of Emtricitabine, Tenofovir Alafenamide and its Metabolite Tenofovir Following Oral Administration of DESCOVY with DRV+COBI in Pediatric Participants with HIV-1 Aged 6 to less than 12 Years and Weighing from 25 to less than 40 kg*

Parameter Mean (CV%)	Emtricitabine*	Tenofovir Alafenamide*	Tenofovir*
C_{max} (microgram per mL)	4.17 (25.9)	0.27† (58.1)	0.06 (12.9)
AUC_{tau} (microgram•h per mL)	29.4 (35.7)	0.53‡ (82.9)	1.11 (15.8)
C_{trough} (microgram per mL)	0.17 (39.4)	NA	0.04 (19.3)

CV = Coefficient of Variation; NA = Not Applicable

* From Intensive PK analysis in a trial of pediatric participants (n=9)

† n=8

‡ n=6

Exposures of FTC and TAF (AUC_{tau} and C_{max}) achieved in 11 pediatric participants with HIV-1 at least 2 years of age and weighing at least 14 to less than 25 kg who received DESCOVY in combination with DRV+COBI were generally higher than exposures achieved in adults; however, the increases were not considered clinically significant (Table 13).

Table 13 Multiple Dose Pharmacokinetic Parameters of Emtricitabine, Tenofovir Alafenamide and its Metabolite Tenofovir Following Oral Administration of DESCOVY with DRV+COBI in Pediatric Participants with HIV-1 at least 2 Years of Age and Weighing from 14 kg to less than 25 kg*

Parameter Mean (CV%)	Emtricitabine*	Tenofovir Alafenamide*	Tenofovir*
C_{max} (microgram per mL)	4.40 (16.5)	0.48† (38.8)	0.06 (36.7)
AUC_{tau} (microgram•h per mL)	22.9 (13.8)	0.43‡ (75.9)	1.05 (38.8)
C_{trough} (microgram per mL)	0.10 (36.7)	NA	0.03 (36.6)

CV = Coefficient of Variation; NA = Not Applicable
* From Intensive PK analysis in a trial of pediatric participants (n=11)
† n=10
‡ n=9

HIV-1 PrEP: The pharmacokinetic data for FTC and TAF following administration of DESCOVY in adolescents without HIV-1 weighing 35 kg and above are not available. The dosage recommendations of DESCOVY for HIV-1 PrEP in this population are based on known pharmacokinetic information in adolescents with HIV-1 taking FTC and TAF for treatment *[see Use in Specific Populations (8.4)].*

Race and Gender

Based on population pharmacokinetic analyses, there are no clinically meaningful differences based on race or gender.

Patients with Renal Impairment

The pharmacokinetics of FTC+TAF combined with EVG+COBI in participants with HIV-1 and renal impairment (eGFR 30 to 69 mL per minute by Cockcroft-Gault method), and in participants with HIV-1 and ESRD (eGFR less than 15 mL per minute by Cockcroft-Gault method) receiving chronic hemodialysis were evaluated in subsets of virologically-suppressed participants in open-label trials. The pharmacokinetics of TAF were similar among healthy participants, participants with HIV-1 and mild or moderate renal impairment, and participants with HIV-1 and ESRD receiving chronic hemodialysis; increases in FTC and TFV exposures in participants with HIV-1 and renal impairment were not considered clinically relevant (Table 14).

Table 14 Pharmacokinetics of the Components of DESCOVY and a Metabolite of TAF (Tenofovir) in Adults with HIV-1 and Renal Impairment Compared to Participants with HIV-1 and Normal Renal Function

	AUC_{tau} (microgram·hour per mL) Mean (CV%)			
Estimated Creatinine Clearance*	**≥90 mL per minute (N=18)†**	**60–89 mL per minute (N=11)‡**	**30–59 mL per minute (N=18)§**	**<15 mL per minute (N=12)¶**
Emtricitabine	11.4 (11.9)	17.6 (18.2)	23.0 (23.6)	62.9 (48.0)#
Tenofovir	0.32 (14.9)	0.46 (31.5)	0.61 (28.4)	8.72 (39.4)Þ

* By Cockcroft-Gault method.
† From a phase 2 trial in adults with HIV-1 and normal renal function treated with FTC+TAF with EVG+COBI.
‡ These participants had an eGFR ranging from 60 to 69 mL per minute.
§ From a phase 3 trial in adults with HIV-1 and renal impairment treated with FTC+TAF with EVG+COBI.
¶ From a phase 3 trial in adults with HIV-1 and ESRD receiving chronic hemodialysis treated with FTC+TAF with EVG+COBI; PK assessed prior to hemodialysis following 3 consecutive daily doses of FTC+TAF with EVG+COBI.
# N = 11.
Þ N = 10.

Patients with Hepatic Impairment

Emtricitabine: The pharmacokinetics of FTC has not been studied in participants with hepatic impairment; however, FTC is not significantly metabolized by liver enzymes, so the impact of hepatic impairment should be limited.

Tenofovir Alafenamide: Clinically relevant changes in tenofovir pharmacokinetics in participants with hepatic impairment were not observed in participants with mild to moderate (Child-Pugh Class A and B) hepatic impairment *[see Use in Specific Populations (8.7)]*.

Hepatitis B and/or Hepatitis C Virus Infection

The pharmacokinetics of FTC and TAF have not been fully evaluated in participants with hepatitis B and/or C virus.

Drug Interaction Studies

The effects of coadministered drugs on the exposure of TAF are shown in Table 15 and the effects of DESCOVY or its components on the exposure of coadministered drugs are shown in Table 16 [these studies were conducted with DESCOVY or the components of DESCOVY (FTC or TAF) administered alone]. For information regarding clinical recommendations, *see Drug Interactions (7)*.

Table 15 Drug Interactions: Changes in TAF Pharmacokinetic Parameters in the Presence of Coadministered Drug(s)*

	Coadministered Drug(s)	**Tenofovir Alafenamide**		**Mean Ratio of TAF PK Parameters**

Coadministered Drug	Coadministered Drug(s) Dosage (once daily) (mg)	Tenofovir Alafenamide Dosage (once daily) (mg)	N	Mean Ratio of Coadministered Drug PK Parameters (90% CI); No effect = 1.00		
				C_{max}	AUC	C_{min}
Atazanavir	300 (+100 ritonavir)	10	10	1.77 (1.28, 2.44)	1.91 (1.55, 2.35)	NC
Cobicistat	150	8	12	2.83 (2.20, 3.65)	2.65 (2.29, 3.07)	NC
Darunavir	800 (+150 cobicistat)	25†	11	0.93 (0.72, 1.21)	0.98 (0.80, 1.19)	NC
Darunavir	800 (+100 ritonavir)	10	10	1.42 (0.96, 2.09)	1.06 (0.84, 1.35)	NC
Dolutegravir	50	10	10	1.24 (0.88, 1.74)	1.19 (0.96, 1.48)	NC
Efavirenz	600	40†	11	0.78 (0.58, 1.05)	0.86 (0.72, 1.02)	NC
Lopinavir	800 (+200 ritonavir)	10	10	2.19 (1.72, 2.79)	1.47 (1.17, 1.85)	NC
Rilpivirine	25	25	17	1.01 (0.84, 1.22)	1.01 (0.94, 1.09)	NC
Sertraline	50 (dosed as a single dose)	10‡	19	1.00 (0.86, 1.16)	0.96 (0.89, 1.03)	NC

NC=Not Calculated

* All interaction studies conducted in healthy participants.
† Study conducted with DESCOVY (FTC/TAF).
‡ Study conducted with FTC+TAF with EVG+COBI.

Table 16 Drug Interactions: Changes in PK Parameters for Coadministered Drug in the Presence of DESCOVY or the Individual Components*

Coadministered Drug	Coadministered Drug Dosage (once daily) (mg)	Tenofovir Alafenamide Dosage (once daily) (mg)	N	Mean Ratio of Coadministered Drug PK Parameters (90% CI); No effect = 1.00		
				C_{max}	AUC	C_{min}
	300 +100			0.98	0.99	1.00

Atazanavir	300 +100 ritonavir	10	10	(0.89, 1.07)	(0.96, 1.01)	(0.96, 1.04)
Darunavir	800 +150 cobicistat	25†	11	1.02 (0.96, 1.09)	0.99 (0.92, 1.07)	0.97 (0.82, 1.15)
Darunavir	800 +100 ritonavir	10	10	0.99 (0.91, 1.08)	1.01 (0.96, 1.06)	1.13 (0.95, 1.34)
Dolutegravir	50 mg	10	10	1.15 (1.04, 1.27)	1.02 (0.97, 1.08)	1.05 (0.97, 1.13)
Lopinavir	800 +200 ritonavir	10	10	1.00 (0.95, 1.06)	1.00 (0.92, 1.09)	0.98 (0.85, 1.12)
Midazolam‡	2.5 (single dose, orally)	25	18	1.02 (0.92, 1.13)	1.13 (1.04, 1.23)	NC
	1 (single dose, intravenous)			0.99 (0.89, 1.11)	1.08 (1.04, 1.14)	NC
Rilpivirine	25	25	16	0.93 (0.87, 0.99)	1.01 (0.96, 1.06)	1.13 (1.04, 1.23)
Sertraline	50 (single dose)	10§	19	1.14 (0.94, 1.38)	0.93 (0.77, 1.13)	NC

NC=Not Calculated

* All interaction studies conducted in healthy participants.
† Study conducted with DESCOVY (FTC/TAF).
‡ A sensitive CYP3A4 substrate.
§ Study conducted with FTC+TAF with EVG+COBI.

12.4 Microbiology

Mechanism of Action

Emtricitabine: FTC, a synthetic nucleoside analog of cytidine, is phosphorylated by cellular enzymes to form emtricitabine 5'-triphosphate. Emtricitabine 5'-triphosphate inhibits the activity of the HIV-1 reverse transcriptase by competing with the natural substrate deoxycytidine 5'-triphosphate and by being incorporated into nascent viral DNA which results in chain termination. Emtricitabine 5′-triphosphate is a weak inhibitor of mammalian DNA polymerases α, β, Ɛ, and mitochondrial DNA polymerase γ.

Tenofovir Alafenamide: TAF is a phosphonoamidate prodrug of tenofovir (2’-deoxyadenosine monophosphate analog). Plasma exposure to TAF allows for permeation into cells and then TAF is intracellularly converted to tenofovir through hydrolysis by cathepsin A. Tenofovir is subsequently phosphorylated by cellular kinases to the active metabolite tenofovir diphosphate. Tenofovir diphosphate inhibits HIV-1 replication through incorporation into viral DNA by the HIV reverse transcriptase, which results in DNA chain-termination.

Tenofovir has activity against HIV-1. Cell culture studies have shown that both tenofovir and FTC can be fully phosphorylated when combined in cells. Tenofovir diphosphate is a weak inhibitor of mammalian DNA polymerases that include mitochondrial DNA polymerase γ and there is no evidence of toxicity to mitochondria in cell culture.

Antiviral Activity in Cell Culture

Emtricitabine: The antiviral activity of FTC against laboratory and clinical isolates of HIV-1 was assessed in T lymphoblastoid cell lines, the MAGI-CCR5 cell line, and primary peripheral blood mononuclear cells. The EC_{50} values for FTC were in the range of 1.3–640 nM. FTC displayed antiviral activity in cell culture against HIV-1 clades A, B, C, D, E, F, and G (EC_{50} values ranged from 7-75 nM) and showed strain specific activity against HIV-2 (EC_{50} values ranged from 7–1,500 nM).

In a study of FTC with a broad panel of representatives from the major classes of approved anti-HIV agents (NRTIs, non-nucleoside reverse transcriptase inhibitors [NNRTIs], integrase strand transfer inhibitors [INSTIs], and PIs) no antagonism was observed for these combinations.

Tenofovir Alafenamide: The antiviral activity of TAF against laboratory and clinical isolates of HIV-1 subtype B was assessed in lymphoblastoid cell lines, PBMCs, primary monocyte/macrophage cells and $CD4^+$-T lymphocytes. The EC_{50} values for TAF ranged from 2.0 to 14.7 nM.

TAF displayed antiviral activity in cell culture against all HIV-1 groups (M, N, O), including sub-types A, B, C, D, E, F, and G (EC_{50} values ranged from 0.10 to 12.0 nM) and strain specific activity against HIV-2 (EC_{50} values ranged from 0.91 to 2.63 nM).

In a study of TAF with a broad panel of representatives from the major classes of approved anti-HIV agents (NRTIs, NNRTIs, INSTIs, and PIs) no antagonism was observed for these combinations.

Prophylactic Activity in a Nonhuman Primate Model of HIV-1 Transmission

Emtricitabine and Tenofovir Alafenamide: The prophylactic activity of the combination of oral FTC and TAF was evaluated in a controlled study of macaques administered once weekly intra-rectal inoculations of chimeric simian/human immunodeficiency type 1 virus (SHIV) for up to 19 weeks (n=6). All 6 macaques that received FTC and TAF at doses resulting in PBMC exposures consistent with those achieved in humans administered a dose of FTC/TAF 200/25 mg remained SHIV uninfected.

Resistance

In Cell Culture

Emtricitabine: HIV-1 isolates with reduced susceptibility to FTC were selected in cell culture and in participants treated with FTC. Reduced susceptibility to FTC was associated with M184V or I substitutions in HIV-1 RT.

Tenofovir Alafenamide: HIV-1 isolates with reduced susceptibility to TAF were selected in cell culture. HIV-1 isolates selected by TAF expressed a K65R substitution in HIV-1 RT, sometimes in the presence of S68N or L429I substitutions; in addition, a K70E substitution in HIV-1 RT was observed.

In Clinical Trials

Treatment of HIV-1

The resistance profile of DESCOVY in combination with other antiretroviral agents for the treatment of HIV-1 infection is based on studies of FTC+TAF with EVG+COBI in the treatment of HIV-1 infection. In a pooled analysis of antiretroviral-naïve participants, genotyping was performed on plasma HIV-1 isolates from all participants with HIV-1 RNA greater than 400 copies per mL at confirmed virologic failure, at Week 48, or at time of early study drug discontinuation. Genotypic resistance developed in 7 of 14 evaluable participants. The resistance-associated substitutions that emerged were M184V/I (N=7) and K65R (N=1). Three participants had virus with emergent R, H, or E at the polymorphic Q207 residue in reverse transcriptase.

One participant was identified with emergent resistance to FTC (M184M/I) out of 4 virologic failure participants in a clinical study of virologically-suppressed participants who switched from a regimen containing FTC+TDF to FTC+TAF with EVG+COBI (N=799).

HIV-1 PrEP

In the DISCOVER trial of HIV-1 uninfected men and transgender women who have sex with men and who are at risk of HIV-1 infection receiving DESCOVY or TRUVADA for HIV-1 PrEP, genotyping was performed on participants found to be infected during the trial who had HIV-1 RNA ≥400 copies/mL (6 of 7 participants receiving DESCOVY and 13 of 15 participants receiving TRUVADA). The development of FTC resistance-associated substitutions, M184I and/or M184V, was observed in 4 HIV-1 infected participants in the TRUVADA group who had suspected baseline infections.

Cross-Resistance

Emtricitabine: FTC-resistant viruses with the M184V or I substitution were cross-resistant to lamivudine, but retained sensitivity to didanosine, stavudine, tenofovir, and zidovudine.

Viruses harboring substitutions conferring reduced susceptibility to stavudine and zidovudine-thymidine analog substitutions (M41L, D67N, K70R, L210W, T215Y/F, K219Q/E) or didanosine (L74V) remained sensitive to FTC. HIV-1 containing the K103N substitution or other substitutions associated with resistance to NNRTIs was susceptible to FTC.

Tenofovir Alafenamide: Tenofovir resistance substitutions K65R and K70E result in reduced susceptibility to abacavir, didanosine, emtricitabine, lamivudine, and tenofovir.

HIV-1 with multiple thymidine analog substitutions (M41L, D67N, K70R, L210W, T215F/Y, K219Q/E/N/R), or multinucleoside resistant HIV-1 with a T69S double insertion mutation or with a Q151M substitution complex including K65R, showed reduced susceptibility to TAF in cell culture.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Emtricitabine

In long-term carcinogenicity studies of FTC, no drug-related increases in tumor incidence were found in mice at doses up to 750 mg per kg per day (23 times the human systemic

exposure at the recommended dose of 200 mg per day in DESCOVY) or in rats at doses up to 600 mg per kg per day (28 times the human systemic exposure at the recommended dose in DESCOVY).

FTC was not genotoxic in the reverse mutation bacterial test (Ames test), mouse lymphoma or mouse micronucleus assays.

FTC did not affect fertility in male rats at approximately 140 times or in male and female mice at approximately 60 times higher exposures (AUC) than in humans given the recommended 200 mg daily dosage in DESCOVY. Fertility was normal in the offspring of mice exposed daily from before birth (in utero) through sexual maturity at daily exposures (AUC) of approximately 60 times higher than human exposures at the recommended 200 mg daily dosage in DESCOVY.

Tenofovir Alafenamide

Since TAF is rapidly converted to tenofovir and a lower tenofovir exposure in rats and mice was observed after TAF administration compared to TDF administration, carcinogenicity studies were conducted only with TDF. Long-term oral carcinogenicity studies of TDF in mice and rats were carried out at exposures up to approximately 10 times (mice) and 4 times (rats) those observed in humans at the recommended dose of TDF (300 mg) for HIV-1 infection. The tenofovir exposure in these studies was approximately 167 times (mice) and 55 times (rat) those observed in humans after administration of the daily recommended dose of DESCOVY. At the high dose in female mice, liver adenomas were increased at tenofovir exposures approximately 10 times (300 mg TDF) and 167 times (DESCOVY) the exposure observed in humans. In rats, the study was negative for carcinogenic findings.

TAF was not genotoxic in the reverse mutation bacterial test (Ames test), mouse lymphoma or rat micronucleus assays.

There were no effects on fertility, mating performance, or early embryonic development when TAF was administered to male rats at a dose equivalent to 62 times (25 mg TAF) the human dose based on body surface area comparisons for 28 days prior to mating and to female rats for 14 days prior to mating through Day 7 of gestation.

13.2 Animal Toxicology and/or Pharmacology

Minimal to slight infiltration of mononuclear cells in the posterior uvea was observed in dogs with similar severity after three- and nine-month administration of TAF; reversibility was seen after a three-month recovery period. No eye toxicity was observed in the dog at systemic exposures of 5 (TAF) and 15 (tenofovir) times the exposure seen in humans with the recommended daily TAF dose in DESCOVY.

14 CLINICAL STUDIES

14.1 Overview of Clinical Trials

The efficacy and safety of DESCOVY have been evaluated in the trials summarized in Table 17.

Table 17 Trials Conducted with FTC+TAF-Containing Products for HIV-1 Treatment and DESCOVY for HIV-1

PrEP

Trial	Population	Study Arms (N)	Timepoint
Study 104 * (NCT01780506) Study 111 * (NCT01797445)	Treatment-naïve adults with HIV-1	FTC+TAF with EVG+COBI † (866) FTC+TDF with EVG+COBI ‡ (867)	48 Weeks
Study 109 § (NCT01815736)	Virologically-suppressed ¶ adults with HIV-1	FTC+TAF with EVG+COBI † (799) ATRIPLA® or TRUVADA®+ATV+COBI or ritonavir or FTC+TDF with EVG+COBI ‡ (397)	48 Weeks
Study 112 # (NCT01818596)	Virologically-suppressed ¶ adults with HIV-1 and renal impairment Þ	FTC+TAF with EVG+COBI † (242)	24 Weeks
Study 1825 # (NCT02600819)	Virologically-suppressed ¶ adults with HIV-1 and ESRD ß receiving chronic hemodialysis	FTC+TAF with EVG+COBI † (55)	48 Weeks
Study 106 # (Cohort 1) (NCT01854775)	Treatment-naïve adolescents with HIV-1 between the ages of 12 to less than 18 years (at least 35 kg)	FTC+TAF with EVG+COBI † (50)	48 Weeks
Study 106 # (Cohort 2) (NCT01854775)	Virologically-suppressed ¶ children with HIV-1 between the ages of 6 to less than 12 years (at least 25 kg)	FTC+TAF with EVG+COBI † (52)	48 Weeks
Study 1474 # (Cohort 3)	Virologically-suppressed ¶ children with HIV-1 at least 2 years (at	FTC+TAF with bictegravir à (22)	24 Weeks

(NCT02881320)	2 years (at least 14 kg and less than 25 kg)	bictegravir ß (22)	
Study 128 # (Cohort 2) (NCT02016924)	Virologically-suppressed ¶ children with HIV-1 between the ages of 6 to less than 12 years (at least 25 kg and less than 40 kg)	DESCOVY with DRV+COBI (9)	48 Weeks
Study 128 # (Cohort 3) (NCT02016924)	Virologically-suppressed ¶ children with HIV-1 at least 2 years (at least 14 kg and less than 25 kg)	DESCOVY with DRV+COBI (11)	48 Weeks
DISCOVER * (NCT02842086)	Men or transgender women without HIV-1 who have sex with men	DESCOVY (2,670) TRUVADA® (2,665)	4,370 person-years è

* Randomized, double-blind, active-controlled study.
† Administered as GENVOYA®.
‡ Administered as STRIBILD®.
§ Randomized, open-label, active controlled trial.
¶ HIV-1 RNA less than 50 copies per mL.
# Open label trial.
Þ Estimated creatinine clearance between 30 and 69 mL per minute by Cockcroft-Gault method.
ß End stage renal disease (estimated creatinine clearance of less than 15 mL per minute by Cockcroft-Gault method).
à Administered as BIKTARVY®.
è Exposure in the DESCOVY group.

14.2 Clinical Trial Results for Treatment of HIV-1

Clinical Trials in Adults with HIV-1

In trials of FTC+TAF with EVG+COBI in adults with HIV-1 as initial therapy in those with no antiretroviral treatment history (N=866) and to replace a stable antiretroviral regimen in those who were virologically-suppressed for at least 6 months with no known resistance substitutions (N=799), 92% and 96% of participants in the two populations, respectively, had HIV-1 RNA less than 50 copies per mL at Week 48.

Clinical Trials in Pediatric Patients with HIV-1

Study 106:

An open-label, single arm trial of FTC+TAF with EVG+COBI enrolled 50 treatment-naïve adolescents with HIV-1 aged 12 to less than 18 years weighing at least 35 kg (cohort 1) and 52 virologically suppressed children with HIV-1 aged 6 to less than 12 years weighing at least 25 kg (cohort 2). In cohort 1, the virologic response rate (i.e., HIV-1 RNA less than 50 copies per mL) was 92% (46/50) and the mean increase from baseline in CD4+ cell count was 224 cells per mm^3 at Week 48. In cohort 2, 98% (51/52) of participants remained virologically suppressed at Week 48. From a mean (SD) baseline CD4+ cell count of 961 (275.5) cells per mm^3, the mean change from baseline in CD4+ cell count was -66 cells per mm^3 and the mean (SD) change in CD4% was -0.6% (4.4%) at Week 48. All participants maintained CD4+ cell counts above 400 cells/mm^3 *[see Adverse Reactions (6.1) and Use in Specific Populations (8.4)].*

Study 1474:

In a separate open-label single arm trial of FTC+TAF with bictegravir that enrolled 24 virologically-suppressed children at least 2 years of age and weighing at least 14 to less than 25 kg (cohort 3), 91% (20/22) of participants remained virologically suppressed at Week 24. From a mean (SD) baseline CD4+ count of 1104 (440), the mean (SD) change from baseline in CD4+ cell count was −126 (264) cells per mm^3, and the mean (SD) change in CD4% was 0.2% (4.4%) at Week 24.

Study 128:

In a separate open-label trial DESCOVY was administered in combination with DRV+COBI to virologically-suppressed pediatric participants with HIV-1. In cohort 2 of this trial in 9 pediatric participants aged 6 to less than 12 years and weighing at least 25 to less than 40 kg, 100% (9/9) remained virologically-suppressed at Week 48. In cohort 2, from a mean (SD) baseline CD4+ count of 898 (209), the mean (SD) change from baseline in CD4+ cell count was 10 (199) cells per mm^3 and the mean (SD) change in CD4% was 1.26% (4.8%) at Week 48. In cohort 3 of this trial in 11 pediatric participants at least 2 years of age and weighing 14 to less than 25 kg, 91% (10/11) remained virologically-suppressed at Week 48.In cohort 3, from a mean (SD) CD4+ count of 1185 (317), the mean (SD) change from baseline in CD4+ cell count was -122 (329) cells per mm^3 and the mean (SD) change in CD4% was 1.4% (2.5%) at Week 48.

Clinical Trials in Adults with HIV-1 and Renal Insufficiency

In a trial in 248 adults with HIV-1 and estimated creatinine clearance greater than 30 mL per minute but less than 70 mL per minute, 95% (235/248) of the combined population of treatment-naïve participants began on FTC+TAF with EVG+COBI (N=6) and those previously virologically-suppressed on other regimens and switched to FTC+TAF with EVG+COBI (N=242) had HIV-1 RNA less than 50 copies per mL at Week 24.

In a trial in 55 virologically-suppressed adults with HIV-1 and ESRD (estimated creatinine clearance of less than 15 mL per minute) receiving chronic hemodialysis for at least 6 months who switched to FTC+TAF with EVG+COBI, 82% (45/55) maintained HIV-1 RNA less than 50 copies per mL at Week 48. Two participants had HIV-1 RNA ≥ 50 copies per mL by Week 48, 7 discontinued due to AE or other reasons while suppressed, and 1 did not have an HIV-1 RNA measurement at Week 48.

14.3 Clinical Trial Results for HIV-1 PrEP

The efficacy and safety of DESCOVY to reduce the risk of acquiring HIV-1 infection were evaluated in a randomized, double-blind multinational trial (DISCOVER) in HIV-seronegative men (N=5,262) or transgender women (N=73) who have sex with men and are at risk of HIV-1 infection, comparing once daily DESCOVY (N=2,670) to TRUVADA (FTC/TDF 200 mg/300 mg; N=2,665). Evidence of risk behavior at entry into the trial included at least 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. The median age of participants was 34 years (range, 18-76); 84% were White, 9% Black/Mixed Black, 4% Asian, and 24% Hispanic/Latino. At baseline, 897 participants (17%) reported receiving TRUVADA for PrEP.

At weeks 4, 12, and every 12 weeks thereafter, all participants received local standard of care HIV-1 prevention services, including HIV-1 testing, evaluation of adherence, safety evaluations, risk-reduction counseling, condoms, management of sexually transmitted infections, and assessment of sexual behavior.

Trial participants maintained a high risk of sexual HIV-1 acquisition, with high rates of rectal gonorrhea (DESCOVY, 24%; TRUVADA, 25%), rectal chlamydia (DESCOVY, 30%; TRUVADA, 31%), and syphilis (14% in both treatment groups) during the trial.

The primary outcome was the incidence of documented HIV-1 infection per 100 person-years in participants randomized to DESCOVY and TRUVADA (with a minimum follow-up of 48 weeks and at least 50% of participants having 96 weeks of follow-up). DESCOVY was non-inferior to TRUVADA in reducing the risk of acquiring HIV-1 infection (Table 18). The results were similar across the subgroups of age, race, gender identity, and baseline TRUVADA for PrEP use.

Table 18 HIV-1 Infection Results in DISCOVER Trial – Full Analysis Set

	DESCOVY (N=2,670)	**TRUVADA (N=2,665)**	
	4,370 person-years	**4,386 person-years**	**Rate Ratio (95% CI)**
HIV-1 infections, n	7	15	
Rate of HIV-1 infections per 100 person-years	0.16	0.34	0.468 (0.19, 1.15)

CI = Confidence interval.

Of the 22 participants diagnosed with HIV-1 infection in the trial, five had suspected baseline infection prior to study entry (DESCOVY, 1; TRUVADA, 4). In a case-control substudy of intracellular drug levels and estimated number of daily doses as measured by dried blood spot testing, median intracellular tenofovir diphosphate concentrations were substantially lower in participants infected with HIV-1 at the time of diagnosis compared with uninfected matched control participants. For both DESCOVY and TRUVADA, efficacy was therefore strongly correlated to adherence to daily dosing.

16 HOW SUPPLIED/STORAGE AND HANDLING

DESCOVY tablets are available in bottles and blister packs containing 30 tablets:

Bottles

- 200 mg/25 mg tablets each contain 200 mg of emtricitabine (FTC) and 25 mg of tenofovir alafenamide (TAF). These tablets are blue, rectangular-shaped, and film-coated with “GSI” debossed on one side and “225” on the other side (NDC 61958-2002-1).
- 120 mg/15 mg tablets each contain 120 mg of FTC and 15 mg of TAF. These tablets are white, round-shaped, and film coated with “GSI” debossed on one side and “15” on the other side (NDC 61958-2005-1).

Bottles contain a silica gel desiccant, polyester coil, and child resistant closure.

Keep bottle tightly closed.

The bottle containing 200 mg/25 mg tablets (NDC 61958-2002-1) may have a tamper-evident seal over the cap. If a tamper-evident seal is present, do not use if the seal is opened or damaged.

Blister Pack

- 200 mg/25 mg tablets each contain 200 mg of FTC and 25 mg of TAF. These tablets are blue, rectangular-shaped, and film-coated with “GSI” debossed on one side and “225” on the other side (NDC 61958-2002-2).

Blister packs are sealed with a child-resistant laminated foil lidding material (peel-push) and each blister cavity contains a die-cut desiccant film which is heat staked to the foil lidding material.

Store at 25°C (77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) (see USP Controlled Room Temperature).

Dispense only in original container.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Important Information for Individuals Without HIV-1 Taking DESCOVY for HIV-1 PrEP

Advise individuals without HIV-1 about the following *[see Warnings and Precautions (5.2)]:*

- The need to confirm that they are HIV-negative before starting to take DESCOVY to reduce the risk of acquiring HIV-1.
- That HIV-1 resistance substitutions may emerge in individuals with undetected HIV-1 infection who are taking DESCOVY, because DESCOVY alone does not constitute a complete regimen for HIV-1 treatment.
- The importance of taking DESCOVY on a regular dosing schedule and strict adherence to the recommended dosing schedule to reduce the risk of acquiring HIV-1. Individuals without HIV-1 who miss doses are at greater risk of acquiring HIV-1 than those who do not miss doses.
- That DESCOVY does not prevent other sexually acquired infections and should be used as part of a complete prevention strategy including other prevention measures.

- To use condoms consistently and correctly to lower the chances of sexual contact with any body fluids such as semen, vaginal secretions, or blood.
- The importance of knowing their HIV-1 status and the HIV-1 status of their partner(s).
- The importance of virologic suppression in their partner(s) with HIV-1.
- The need to get tested regularly for HIV-1 (at least every 3 months, or more frequently for some individuals such as adolescents) and to ask their partner(s) to get tested as well.
- To report any symptoms of acute HIV-1 infection (flu-like symptoms) to their healthcare provider immediately.
- That the signs and symptoms of acute infection include fever, headache, fatigue, arthralgia, vomiting, myalgia, diarrhea, pharyngitis, rash, night sweats, and adenopathy (cervical and inguinal).
- To get tested for other sexually transmitted infections, such as syphilis, chlamydia, and gonorrhea, that may facilitate HIV-1 transmission.
- To assess their sexual risk behavior and get support to help reduce sexual risk behavior.

Post-treatment Acute Exacerbation of Hepatitis B in Patients with HBV

Inform individuals that severe acute exacerbations of hepatitis B have been reported in patients who are infected with HBV and have discontinued products containing FTC and/or TDF and may likewise occur with discontinuation of DESCOVY *[see Warnings and Precautions (5.1)]*. Advise individuals with HBV to not discontinue DESCOVY without first informing their healthcare provider.

Immune Reconstitution Syndrome

Advise patients with HIV-1 to inform their healthcare provider immediately of any symptoms of infection. In some patients with advanced HIV infection (AIDS), signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment is started *[see Warnings and Precautions (5.3)]*.

New Onset or Worsening Renal Impairment

Advise patients with HIV-1 and individuals without HIV-1 to avoid taking DESCOVY with concurrent or recent use of nephrotoxic agents. Postmarketing cases of renal impairment, including acute renal failure, have been reported *[see Warnings and Precautions (5.4)].*

Lactic Acidosis and Severe Hepatomegaly

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with use of drugs similar to DESCOVY. Advise patients with HIV-1 and individuals without HIV-1 that they should stop DESCOVY if they develop clinical symptoms suggestive of lactic acidosis or pronounced hepatotoxicity *[see Warnings and Precautions (5.5)]*.

Dosage Recommendations for Treatment of HIV-1 Infection

Inform patients with HIV-1 that it is important to take DESCOVY with other antiretroviral drugs for the treatment of HIV-1 on a regular dosing schedule with or without food and to avoid missing doses as it can result in development of resistance *[see Dosage and Administration (2.3, 2.4)]*.

Pregnancy Registry

Inform individuals using DESCOVY that there is an antiretroviral pregnancy registry to monitor fetal outcomes of pregnant women exposed to DESCOVY *[see Use in Specific Populations (8.1)].*

Lactation

Inform individuals with HIV-1 infection that the potential risks of breastfeeding include: (1) HIV-1 transmission to infants without HIV-1, (2) developing viral resistance in infants with HIV-1, and (3) adverse reactions in a breastfed infant similar to those seen in adults *[see Use in Specific Populations (8.2)]*.

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MEDICATION GUIDE
DESCOVY® (des-KOH-vee)
(emtricitabine and tenofovir alafenamide)
tablets

This Medication Guide provides information about two different ways that DESCOVY may be used. See the section **"What is DESCOVY?"** for detailed information about how DESCOVY may be used.

What is the most important information I should know about DESCOVY?
DESCOVY can cause serious side effects, including:

- **Worsening of hepatitis B virus (HBV). Your healthcare provider will test you for HBV before or when you start treatment with DESCOVY. If you have HBV and take DESCOVY, your HBV may get worse (flare-up) if you stop taking DESCOVY. A "flare-up" is when your HBV suddenly returns in a worse way than before.**
  - Do not run out of DESCOVY. Refill your prescription or talk to your healthcare provider before your DESCOVY is all gone.
  - Do not stop taking DESCOVY without first talking to your healthcare provider.
  - If you stop taking DESCOVY, your healthcare provider will need to check your health often and do blood tests regularly for several months to check your liver, and may give you a medicine to treat hepatitis B. Tell your healthcare provider about any new or unusual symptoms you may have after you stop taking DESCOVY.

For more information about side effects, see the section "What are the possible side effects of DESCOVY?"

Other important information for people who take DESCOVY to help reduce their risk of getting human immunodeficiency virus-1 (HIV-1), also called pre-exposure prophylaxis or "PrEP":

Before taking DESCOVY to reduce your risk of getting HIV-1:

- **You must be HIV-1 negative to start DESCOVY. You must get tested to make sure that you do not already have HIV-1.**

- **Do not take DESCOVY for HIV-1 PrEP unless you are confirmed to be HIV-1 negative.**
- Some HIV-1 tests can miss HIV-1 in a person who has recently become infected. If you have flu-like symptoms, you could have recently become infected with HIV-1. Tell your healthcare provider if you had a flu-like illness within the last month before starting DESCOVY or at any time while taking DESCOVY. Symptoms of new HIV-1 include:

  - tiredness
  - fever
  - joint or muscle aches
  - headache
  - sore throat
  - vomiting or diarrhea
  - rash
  - night sweats
  - enlarged lymph nodes in the neck or groin

While you are taking DESCOVY for HIV-1 PrEP:

- **DESCOVY does not prevent other sexually transmitted infections (STIs). Practice safer sex by using a latex or polyurethane condom to reduce the risk of getting STIs.**
- **You must stay HIV-1 negative to keep taking DESCOVY for HIV-1 PrEP.**
  - Know your HIV-1 status and the HIV-1 status of your partners.
  - Ask your partners with HIV-1 if they are taking HIV-1 medicines and have an undetectable viral load. An undetectable viral load is when the amount of virus in the blood is too low to be measured in a lab test. To maintain an undetectable viral load, your partners must keep taking HIV-1 medicines every day. Your risk of getting HIV-1 is lower if your partners with HIV-1 are taking effective treatment.
  - Get tested for HIV-1 at least every 3 months or when your healthcare provider tells you.
  - Get tested for other STIs such as syphilis, chlamydia, and gonorrhea. These infections make it easier for HIV-1 to infect you.
  - If you think you were exposed to HIV-1, tell your healthcare provider right away. They may want to do more tests to be sure you are still HIV-1 negative.
  - Get information and support to help reduce sexual risk behaviors.
  - Do not miss any doses of DESCOVY. Missing doses increases your risk of getting HIV-1.
- If you do become HIV-1 positive, you need more medicine than DESCOVY alone to treat HIV-1. DESCOVY by itself is not a complete treatment for HIV-1.

If you have HIV-1 and take only DESCOVY, over time your HIV-1 may become harder to treat.

What is DESCOVY?

DESCOVY is a prescription medicine that may be used in two different ways. DESCOVY is used:

- to treat HIV-1
  - in adults and children who weigh at least 77 pounds (35 kg) together with other HIV-1 medicines.
  - in children who weigh at least 31 pounds (14 kg) and less than 77 pounds (35 kg) together with certain other HIV-1 medicines. Your healthcare provider will determine which other HIV-1 medicines may be used with DESCOVY.
- for HIV-1 PrEP to reduce the risk of getting HIV-1 in adults and adolescents who

weigh at least 77 pounds (35 kg). It is not known if DESCOVY is effective in reducing the risk of getting HIV-1 from certain types of sex.
    - DESCOVY for PrEP is not for use in people born female (assigned female at birth) who are at risk of getting HIV-1 from vaginal sex, because its effectiveness has not been studied.

HIV-1 is the virus that causes Acquired Immune Deficiency Syndrome (AIDS).
DESCOVY contains the prescription medicines emtricitabine and tenofovir alafenamide.
It is not known if DESCOVY for treatment of HIV-1 is safe and effective in children who weigh less than 31 pounds (14 kg).
It is not known if DESCOVY is safe and effective in reducing the risk of HIV-1 in people who weigh less than 77 pounds (35 kg).

For people taking DESCOVY for HIV-1 PrEP:
Do not take DESCOVY for HIV-1 PrEP if:

- **you already have HIV-1.** If you are HIV-1 positive, you need to take other medicines with DESCOVY to treat HIV-1. DESCOVY by itself is not a complete treatment for HIV-1.
- **you do not know your HIV-1 status.** You may already be HIV-1 positive. You need to take other HIV-1 medicines with DESCOVY to treat HIV-1.

DESCOVY can only help reduce your risk of getting HIV-1 **before** you are infected.

What should I tell my healthcare provider before taking DESCOVY?
Before taking DESCOVY, tell your healthcare provider about all of your medical conditions, including if you:

- have liver problems, including HBV
- have kidney problems
- are pregnant or plan to become pregnant. It is not known if DESCOVY can harm your unborn baby. Tell your healthcare provider if you become pregnant during treatment with DESCOVY.
  Pregnancy Registry: There is a pregnancy registry for people who take DESCOVY during pregnancy. The purpose of this registry is to collect information about the health of you and your baby. Talk with your healthcare provider about how you can take part in this registry.
- are breastfeeding or plan to breastfeed. DESCOVY passes to your baby in your breast milk. Talk to your healthcare provider about the following risks to your baby from breastfeeding during treatment with DESCOVY:
    - the HIV-1 virus may pass to your baby if your baby does not have HIV-1.
    - the HIV-1 virus may become harder to treat if your baby has HIV-1.
    - your baby may get side effects from DESCOVY.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.
Some medicines may interact with DESCOVY. Keep a list of your medicines and show it to your healthcare provider and pharmacist when you get a new medicine.

- You can ask your healthcare provider or pharmacist for a list of medicines that interact with DESCOVY.
- **Do not start a new medicine without telling your healthcare provider.** Your healthcare provider can tell you if it is safe to take DESCOVY with other medicines.

How should I take DESCOVY?

- Take DESCOVY exactly as your healthcare provider tells you to take it. If you take DESCOVY to treat HIV-1, you need to take DESCOVY with other HIV-1 medicines. Your healthcare provider will tell you what medicines to take and how to take them.
- Take DESCOVY 1 time each day with or without food.
- If you are on dialysis, take your daily dose of DESCOVY following dialysis.
- Do not change your dose or stop taking DESCOVY without first talking with your healthcare provider. Stay under a healthcare provider's care when taking DESCOVY. Do not miss a dose of DESCOVY.
- If you take too much DESCOVY, call your healthcare provider or go to the nearest hospital emergency room right away.
- When your DESCOVY supply starts to run low, get more from your healthcare provider or pharmacy.
  - If you are taking DESCOVY for treatment of HIV-1, the amount of virus in your blood may increase if the medicine is stopped for even a short time. The virus may develop resistance to DESCOVY and become harder to treat.
  - If you are taking DESCOVY for HIV-1 PrEP, missing doses increases your risk of getting HIV-1.

What are the possible side effects of DESCOVY?
DESCOVY may cause serious side effects, including:

- **See "What is the most important information I should know about DESCOVY?"**
- **Changes in your immune system (Immune Reconstitution Syndrome)** can happen when you start taking medicines to treat HIV-1. Your immune system may get stronger and begin to fight infections that have been hidden in your body for a long time. Tell your healthcare provider right away if you have any new symptoms of infection after starting your HIV-1 medicine.
- **New or worse kidney problems, including kidney failure.** Your healthcare provider should do blood and urine tests to check your kidneys before you start and while taking DESCOVY. Your healthcare provider may tell you to stop taking DESCOVY if you develop new or worse kidney problems.
- **Too much lactic acid in your blood (lactic acidosis).** Too much lactic acid is a serious but rare medical emergency that can lead to death. Tell your healthcare provider right away if you get these symptoms: weakness or being more tired than usual, unusual muscle pain, being short of breath or fast breathing, stomach pain with nausea and vomiting, cold or blue hands and feet, feel dizzy or lightheaded, or a fast or abnormal heartbeat.
- **Severe liver problems.** In rare cases, severe liver problems can happen that can lead to death. Tell your healthcare provider right away if you get these symptoms: skin or the white part of your eyes turns yellow, dark "tea-colored" urine, light-colored stools, loss of appetite for several days or longer, nausea, or stomach-area pain.

The most common side effect of DESCOVY for treatment of HIV-1 is nausea.
The most common side effect of DESCOVY for HIV-1 PrEP is diarrhea.
These are not all of the possible side effects of DESCOVY.
Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store DESCOVY?

- Store DESCOVY at room temperature between 68°F to 77°F (20°C to 25°C).
- Keep DESCOVY in its original bottle or blister pack.
- Keep the bottle tightly closed.
- The bottle containing 200 mg/25 mg tablets may have a tamper-evident seal over the cap. If a tamper-evident seal is present, do not use if the seal is opened or damaged.

Keep DESCOVY and all medicines out of reach of children.

General information about the safe and effective use of DESCOVY.
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use DESCOVY for a condition for which it was not prescribed. Do not give DESCOVY to other people, even if they have the same symptoms you have. It may harm them. You can ask your healthcare provider or pharmacist for information about DESCOVY that is written for health professionals.

What are the ingredients in DESCOVY?
Active ingredients: emtricitabine and tenofovir alafenamide.
Inactive ingredients: croscarmellose sodium, magnesium stearate, and microcrystalline cellulose.
The 200 mg/25 mg tablets are film-coated with a coating material containing indigo carmine aluminum lake, polyethylene glycol, polyvinyl alcohol, talc, and titanium dioxide.
The 120 mg/15 mg tablets are film-coated with a coating material containing polyvinyl alcohol, titanium dioxide, polyethylene glycol, and talc.
Manufactured and distributed by: Gilead Sciences, Inc. Foster City, CA 94404
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208215-GS-011
For more information, call 1-800-445-3235 or go to www.DESCOVY.com.

This Medication Guide has been approved by the U.S. Food and Drug Administration Revised: 07/2026

PRINCIPAL DISPLAY PANEL - 200 mg/25 mg Tablet Bottle Label

NDC 61958- **2002**-1

30 tablets

Descovy ®

(emtricitabine and tenofovir

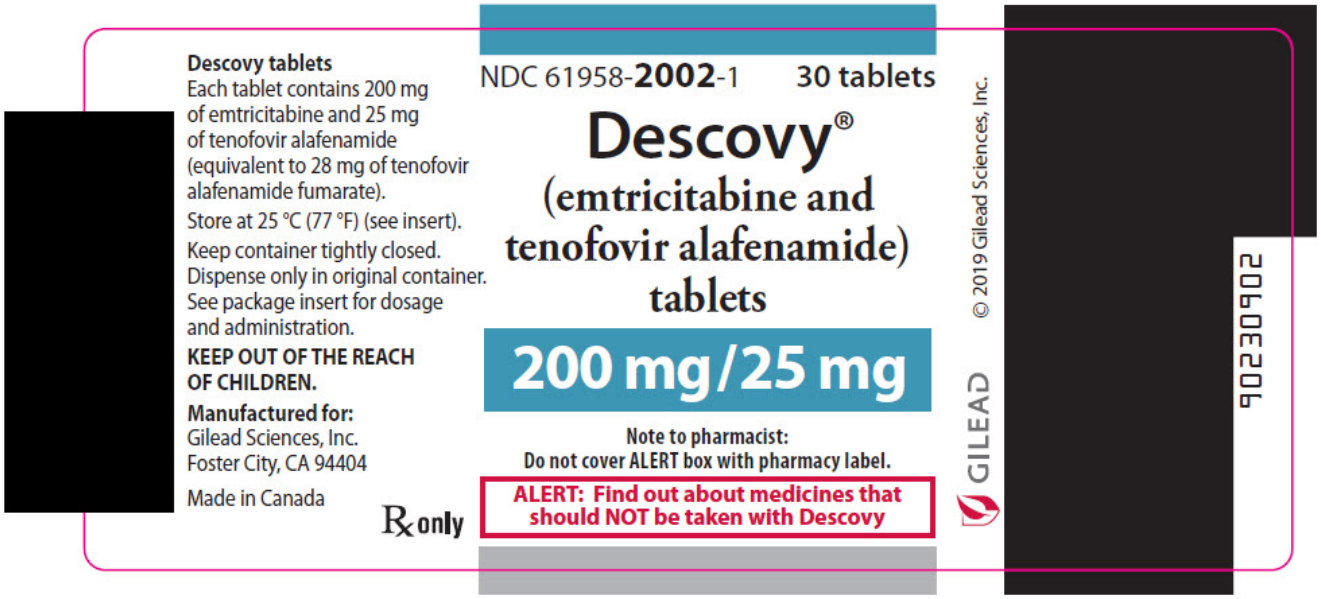
alafenamide) Tablets

200 mg/25 mg

Note to pharmacist: Do not cover ALERT box with pharmacy label.

ALERT: Find out about medicines that

should NOT be taken with Discovy ®



PRINCIPAL DISPLAY PANEL - 30 Tablet Blister Pack

NDC 61958-2002-2

30 tablet blister pack

Descovy®

(emtricitabine and

tenofovir alafenamide) tablets

200 mg / 25 mg

Rx only

Note to pharmacist:

Do not cover ALERT box with pharmacy label.

ALERT: Find out about medicines that

should NOT be taken with Descovy



PRINCIPAL DISPLAY PANEL - 120 mg/15 mg Tablet Bottle Label

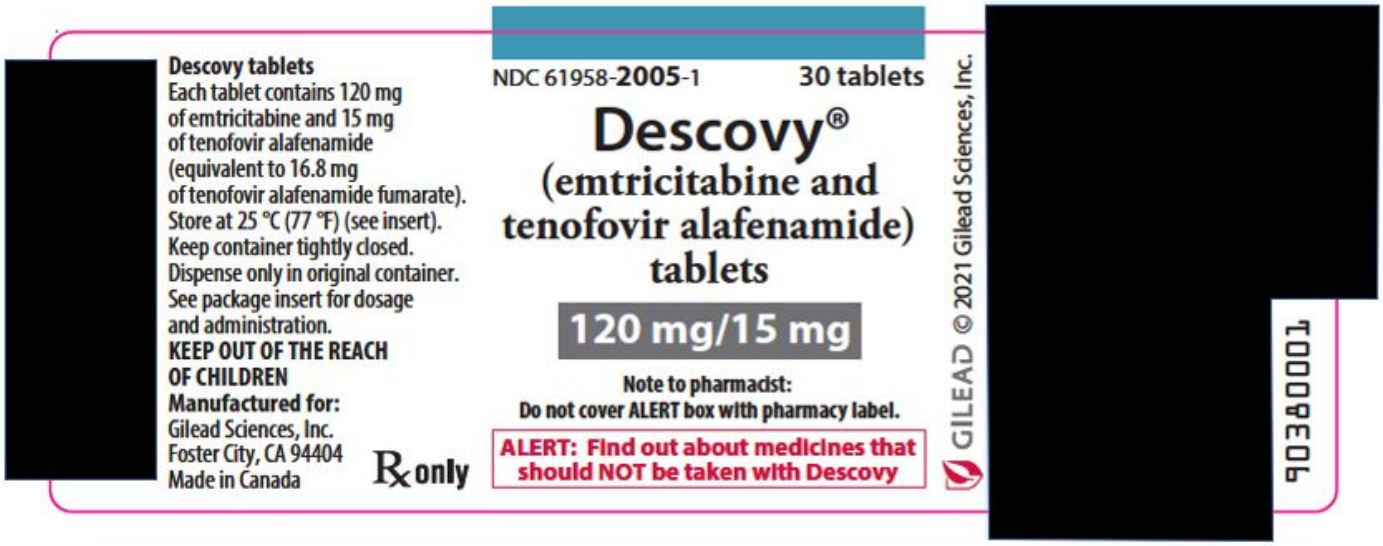
NDC 61958-2005-1
30 tablets

Descovy®
(emtricitabine and
tenofovir alafenamide)
tablets

120 mg/15 mg

Note to pharmacist:
Do not cover ALERT box with pharmacy label.

ALERT: Find out about medicines that
should NOT be taken with Descovy



DESCOVY

emtricitabine and tenofovir alafenamide tablet

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:61958-2002
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
EMTRICITABINE (UNII: G70B4ETF4S) (EMTRICITABINE - UNII:G70B4ETF4S)	EMTRICITABINE	200 mg
TENOFOVIR ALAFENAMIDE FUMARATE (UNII: FWF6Q91TZO) (TENOFOVIR ANHYDROUS - UNII:W4HFE001U5)	TENOFOVIR ALAFENAMIDE	25 mg

Inactive Ingredients	
Ingredient Name	**Strength**
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
CROSCARMELLOSE SODIUM (UNII: M28OL1HH48)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
WATER (UNII: 059QF0KO0R)	
POLYVINYL ALCOHOL, UNSPECIFIED (UNII: 532B59J990)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
POLYETHYLENE GLYCOL 3350 (UNII: G2M7P15E5P)	
TALC (UNII: 7SEV7J4R1U)	
FD&C BLUE NO. 2 (UNII: L06K8R7DQK)	

Product Characteristics			
Color	blue	**Score**	no score
Shape	OVAL (rectangular-shaped)	**Size**	13mm

Flavor		**Imprint Code**	GSI;255
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:61958-2002-1	30 in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product	04/04/2016	
2	NDC:61958-2002-2	30 in 1 BLISTER PACK; Type 0: Not a Combination Product	01/22/2020	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA208215	04/04/2016	

DESCOVY

emtricitabine and tenofovir alafenamide tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:61958-2005
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
EMTRICITABINE (UNII: G70B4ETF4S) (EMTRICITABINE - UNII:G70B4ETF4S)	EMTRICITABINE	120 mg
TENOFOVIR ALAFENAMIDE FUMARATE (UNII: FWF6Q91TZO) (TENOFOVIR ANHYDROUS - UNII:W4HFE001U5)	TENOFOVIR ALAFENAMIDE	15 mg

Inactive Ingredients

Ingredient Name	Strength
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
CROSCARMELLOSE SODIUM (UNII: M28OL1HH48)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
WATER (UNII: 059QF0KO0R)	
POLYVINYL ALCOHOL, UNSPECIFIED (UNII: 532B59J990)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
POLYETHYLENE GLYCOL 3350 (UNII: G2M7P15E5P)	
TALC (UNII: 7SEV7J4R1U)	

Product Characteristics

Color	WHITE	**Score**	no score
Shape	ROUND (round-shaped)	**Size**	8mm
Flavor		**Imprint Code**	GSI;15
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:61958-2005-1	30 in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product	01/07/2022	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA208215	01/07/2022	

Labeler - Gilead Sciences, Inc. (185049848)

Revised: 7/2026 Gilead Sciences, Inc.