Department of Health and Human Services
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Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology
Office of Pharmacovigilance and Epidemiology

Pediatric Postmarketing Pharmacovigilance Review

Date:	May 20, 2025
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Product Name:	Descovy (emtricitabine and tenofovir alafenamide)
Pediatric Labeling Approval Date:	January 7, 2022
Application Type/Number:	NDA 208215
Applicant:	Gilead Sciences, Inc.
TTT Record ID:	2025-14347

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EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Descovy (emtricitabine and tenofovir alafenamide) in pediatric patients less than 18 years of age. The Division of Pharmacovigilance (DPV) conducted this review in accordance with the Pediatric Research Equity Act (PREA). This review focuses on United States (U.S.) serious unlabeled adverse events associated with Descovy in pediatric patients.

Descovy is a two-drug combination of emtricitabine and tenofovir alafenamide, both of which are human immunodeficiency virus type 1 (HIV-1) nucleoside reverse transcriptase inhibitors. Descovy was initially approved in the U.S. on April 4, 2016. Descovy is currently indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients weighing at least 35 kg or in combination with other antiretroviral agents other than protease inhibitors that require a CYP3A inhibitor for the treatment of HIV-1 infection in pediatric patients weighing at least 14 kg and less than 35 kg. Descovy is also 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. Descovy is available in two fixed dose combination tablet strengths: 200 mg/25 mg and 120 mg/15 mg of emtricitabine and tenofovir alafenamide, respectively.

This pediatric postmarketing safety review was prompted by pediatric labeling on January 7, 2022, that expanded the patient population for Descovy to include treatment of HIV-1 infection in pediatric patients at least 2 years of age and weighing at least 14 kg, updated prescribing information with 48 week safety and efficacy data for patients weighing at least 25 kg, and added the new dosage strength of Descovy tablets, 120 mg/15 mg.

DPV previously completed three pediatric postmarketing adverse pharmacovigilance reviews for Descovy:[3-5]

- DPV pediatric postmarketing pharmacovigilance review dated March 6, 2018, was presented to the Pediatric Advisory Committee (PAC) via webposting on June 13, 2018
- DPV pediatric postmarketing pharmacovigilance review dated April 15, 2020, was presented to the PAC via webposting on September 1, 2020
- DPV pediatric postmarketing pharmacovigilance review dated August 31, 2022, was presented to the PAC via webposting on April 19, 2023

DPV's prior evaluations did not identify any new safety concerns and recommended return to routine monitoring for adverse events with Descovy.

DPV reviewed all U.S. serious FAERS reports with Descovy in pediatric patients less than 18 years of age from May 30, 2022, through April 23, 2025, and identified one report; however, this report was excluded from further discussion as it described transplacental exposure to Descovy.

There were no new safety signals identified, no increased severity of any labeled adverse events, and no deaths directly associated with Descovy in pediatric patients less than 18 years of age.

DPV will continue routine pharmacovigilance monitoring.

1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Descovy (emtricitabine and tenofovir alafenamide) in pediatric patients less than 18 years of age. The Division of Pharmacovigilance (DPV) conducted this review in accordance with the Pediatric Research Equity Act (PREA). This review focuses on United States (U.S.) serious unlabeled adverse events associated with Descovy in pediatric patients.

1.1 PEDIATRIC REGULATORY HISTORY

Descovy is a two-drug combination of emtricitabine and tenofovir alafenamide, both of which are human immunodeficiency virus type 1 (HIV-1) nucleoside reverse transcriptase inhibitors. Descovy was initially approved in the U.S. on April 4, 2016.[1] Descovy is currently indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients weighing at least 35 kg or in combination with other antiretroviral agents other than protease inhibitors that require a CYP3A inhibitor for the treatment of HIV-1 infection in pediatric patients weighing at least 14 kg and less than 35 kg.[1] Descovy is also 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.[1] Descovy is available in two fixed dose combination tablet strengths: 200 mg/25 mg and 120 mg/15 mg of emtricitabine and tenofovir alafenamide, respectively.

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1.2 RELEVANT LABELED SAFETY INFORMATION

The Descovy labeling contains the following safety information excerpted from the Highlights of Prescribing Information and the *Pediatric Use* subsection.[1] For additional Descovy labeling information, please refer to the full prescribing information.[1]

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 HBV-infected individuals 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)

----------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 HIV-1 infected patients, the most common adverse reaction (incidence greater than or equal to 10%, all grades) was nausea. (6.1)
- In HIV-1 uninfected adults in a PrEP trial, the most common adverse reaction (incidence greater than or equal to 5%, all grades) was diarrhea. (6.1)

----------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)

8.4 Pediatric Use

Treatment of HIV-1 Infection

The safety and effectiveness of DESCOVY, in combination with other antiretroviral agents, for the treatment of HIV-1 infection was established in pediatric patients with body weight greater than or equal to 14 kg *[see Indication and Usage (1.1) and Dosage and Administration (2.3, 2.4)]*.

Use of DESCOVY in pediatric patients between 6 to less than 18 years of age and weighing at least 25 kg is supported by adequate and well controlled studies of FTC+TAF with EVG+COBI in adults and by an open-label trial in antiretroviral treatment-naïve HIV-1 infected pediatric subjects aged 12 to less than 18 years and weighing at least 35 kg through Week 48 (N=50; cohort 1) and in virologically-suppressed pediatric subjects aged 6 to less than 12 years and weighing at least 25 kg through Week 48 (N=52; cohort 2). The safety and efficacy of FTC+TAF with EVG+COBI in adolescent subjects was similar to that in adults on this regimen. The safety and efficacy of FTC+TAF with EVG+COBI in subjects 6 to 12 years of age weighing at least 25 kg was similar to that in antiretroviral treatment-naïve adults and adolescents on this regimen, with the exception of a decrease from baseline in CD4+ cell count *[see Adverse Reactions (6.1), Clinical Pharmacology (12.3) and Clinical Studies (14.2)]*.

Use of DESCOVY in pediatric patients between 2 to less than 6 years of age and weighing at least 14 to less than 25 kg is supported by adequate and well controlled studies of FTC+TAF with EVG+COBI in adults and by a separate open-label trial of FTC+TAF with bictegravir in virologically-suppressed pediatric patients at least 2 years of age and weighing at least 14 to less than 25 kg through Week 24 (N=22; cohort 3). The safety and efficacy of FTC+TAF in these pediatric subjects were similar to that observed in adults who received FTC+TAF with bictegravir *[see Adverse Reactions (6.1), Clinical Pharmacology (12.3) and Clinical Studies (14.2)]*.

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 pediatric patients weighing less than 35 kg *[see Dosage and Administration (2.4)]*.

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 HIV-1 infected adults and pediatric subjects *[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 patients weighing less than 35 kg have not been established.

2 METHODS AND MATERIALS

2.1 FAERS SEARCH STRATEGY

DPV searched the FAERS database with the strategy described in **Table 1**.

Table 1. FAERS Search Strategy*	
Date of search	April 24, 2025
Time period of search	May 30, 2022† - April 23, 2025
Search type	RxLogix Pediatric Focused Review Alert – DPV
Product terms	Product active ingredient: emtricitabine\tenofovir alafenamide, emtricitabine\tenofovir alafenamide fumarate
MedDRA search terms (Version 27.1)	All Preferred Terms

Table 1. FAERS Search Strategy*	
Other criteria	Case Seriousness: Serious‡ Country Derived: USA

* See Appendix A for a description of the FAERS database.
† The FAERS search period for the most recently completed DPV pediatric postmarketing pharmacovigilance review for Descovy ended on May 29, 2022.
‡ For the purposes of this review, the following outcomes qualify as serious: death, life-threatening, hospitalization (initial or prolonged), disability, congenital anomaly, required intervention, or other serious important medical events.
Abbreviations: MedDRA=Medical Dictionary for Regulatory Activities, USA=United States of America

3 RESULTS

3.1 FAERS

3.1.1 Selection of U.S. Serious Pediatric Cases in FAERS

Our FAERS search retrieved one U.S. serious pediatric report for patients less than 18 years old from May 30, 2022, through April 23, 2025.[1] We excluded the report from further discussion as it described transplacental exposure to Descovy.[2]

3.1.2 Summary of U.S. Fatal Pediatric Cases (N=0)

There are no fatal pediatric adverse event cases for discussion.

3.1.3 Summary of U.S. Serious Non-Fatal Pediatric Cases (N=0)

There are no non-fatal pediatric adverse event cases for discussion.

4 DISCUSSION

DPV reviewed all U.S. serious FAERS reports with Descovy in pediatric patients less than 18 years of age from May 30, 2022, through April 23, 2025, and identified one report; however, this report was excluded from further discussion as it described transplacental exposure to Descovy.

There were no new safety signals identified, no increased severity of any labeled adverse events, and no deaths directly associated with Descovy in pediatric patients less than 18 years of age.

5 CONCLUSION

DPV did not identify any new pediatric safety concerns for Descovy at this time and will continue routine pharmacovigilance monitoring for Descovy.

[1] The pediatric report was identified among reports not coded with an age.
[2] The report described a 42-day-old male infant born to a mother of advanced maternal age who was treated with dolutegravir, emtricitabine, and tenofovir alafenamide from before conception until delivery. The infant was delivered at 24 weeks and 5 days gestation and later died from complications of necrotizing enterocolitis.

6 REFERENCES

1. Descovy (emtricitabine and tenofovir alafenamide) [package insert]. Foster City, CA: Gilead Sciences, Inc. January 2022
2. U.S. Food and Drug Administration. Supplemental NDA Approval Letter (S-020) for NDA 208215, Descovy (emtricitabine and tenofovir alafenamide). January 7, 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2022/208215Orig1s020ltr.pdf.
3. Dang V, Kim I, Kapoor R, Diak IL. Descovy Pediatric Postmarketing Pharmacovigilance Review. August 31, 2022. Available at: https://www.fda.gov/media/169185/download.
4. Chamberlain C, Kim I, Cao C, Diak IL. Descovy Pediatric Postmarketing Pharmacovigilance Review. April 15, 2020. Available at: https://www.fda.gov/media/169190/download.
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7 APPENDICES

7.1 APPENDIX A. FDA ADVERSE EVENT REPORTING SYSTEM (FAERS)

The FDA Adverse Event Reporting System (FAERS) is a database that contains information on adverse event and medication error reports submitted to FDA. The database is designed to support FDA's postmarketing safety surveillance program for drug and therapeutic biological products. The informatic structure of the database adheres to the international safety reporting guidance issued by the International Council on Harmonisation. Adverse events and medication errors are coded to terms in the Medical Dictionary for Regulatory Activities terminology. The suspect products are coded to valid tradenames or active ingredients in the FAERS Product Dictionary.

FAERS data have limitations. First, there is no certainty that the reported event was actually due to the product. FDA does not require that a causal relationship between a product and event be proven, and reports do not always contain enough detail to properly evaluate an event. Further, FDA does not receive reports for every adverse event or medication error that occurs with a product. Many factors can influence whether an event will be reported, such as the time a product has been marketed and publicity about an event. Therefore, FAERS data cannot be used to calculate the incidence of an adverse event or medication error in the U.S. population.