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

Pediatric Postmarketing Pharmacovigilance Review

Date:	July 22, 2025
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Product Name:	Vemlidy (tenofovir alafenamide)
Pediatric Labeling Approval Date:	October 17, 2022 and March 27, 2024
Application Type/Number:	NDA 208464
Applicant:	Gilead
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EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for VEMLIDY (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 tenofovir alafenamide in pediatric patients.

VEMLIDY (tenofovir alafenamide) is a nucleoside analog reverse transcriptase inhibitor initially approved in the U.S. on November 10, 2016. Tenofovir alafenamide is currently indicated for the treatment of chronic hepatitis B virus (HBV) infection in adults and pediatric patients 6 years of age and older weighing at least 25 kg with compensated liver disease.

This pediatric postmarketing safety review was prompted by the pediatric labeling on October 17, 2022, that expanded the use of tenofovir alafenamide to include use in patients 12 years of age and older; and the labeling on March 27, 2025, that expanded the indication to include use in patients 6 years and older weighing at least 25 kg.

DPV reviewed all U.S. serious FAERS reports with tenofovir alafenamide in pediatric patients less than 18 years of age from November 10, 2016, to June 10, 2025, and identified four reports; however, all reports were excluded from further discussion as they all described transplacental exposure.

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

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

1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for VEMLIDY (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 tenofovir alafenamide in pediatric patients.

1.1 PEDIATRIC REGULATORY HISTORY

VEMLIDY (tenofovir alafenamide) is a nucleoside analog reverse transcriptase inhibitor initially approved in the U.S. on November 10, 2016.[1] Tenofovir alafenamide is currently indicated for the treatment of chronic hepatitis B virus (HBV) infection in adults and pediatric patients 6 years of age and older weighing at least 25 kg with compensated liver disease.[2]

This pediatric postmarketing safety review was prompted by the pediatric labeling on October 17, 2022, that expanded the tenofovir alafenamide indication to include use in patients 12 years of age and older; and the labeling on March 27, 2024, that expanded the indication to include use in patients 6 years of age and older and weighing at least 25 kg.[3,4]

1.2 RELEVANT LABELED SAFETY INFORMATION

The tenofovir alafenamide labeling contains the following safety information excerpted from the Highlights of Prescribing Information and the *Pediatric Use* subsection.[2] For additional tenofovir alafenamide labeling information, please refer to the full prescribing information.

WARNING: POSTTREATMENT SEVERE ACUTE EXACERBATION OF HEPATITIS B

Discontinuation of anti-hepatitis B therapy, including VEMLIDY, may result in severe acute exacerbations of hepatitis B. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who discontinue anti-hepatitis B therapy, including VEMLIDY. If appropriate, resumption of anti-hepatitis B therapy may be warranted [see Warnings and Precautions (5.1)].

----------CONTRAINDICATIONS----------

None. (4)

---------- WARNINGS AND PRECAUTIONS ----------

- HBV and HIV-1 coinfection: VEMLIDY alone is not recommended for the treatment of HIV-1 infection. HIV-1 resistance may develop in these patients. (5.2)
- New onset or worsening renal impairment: Prior to or when initiating VEMLIDY, and during treatment on a clinically appropriate schedule, assess serum creatinine, estimated creatinine clearance, urine glucose, and urine protein in all patients. Also assess serumphosphorus in patients with chronic kidney disease. (5.3)
- Lactic acidosis/severe hepatomegaly with steatosis: Discontinue treatment in patients who develop symptoms or laboratory findingssuggestive of lactic acidosis or pronounced hepatotoxicity. (5.4)

---------- ADVERSE REACTIONS ----------

Most common adverse reaction (incidence greater than or equal to 10%, all grades) is headache. (6.1)

8.4 Pediatric Use

The pharmacokinetics, safety, and effectiveness of VEMLIDY for the treatment of chronic HBV infection have been established in pediatric patients between the ages of 6 to less than 18 years and weighing at least 25 kg (N=59) in Trial 1092 up to 96 weeks. No clinically meaningful differences in pharmacokinetics or safety were observed in comparison to those observed in adults [see Adverse Reactions (6.1), Clinical Pharmacology (12.3), and Clinical Studies (14.5)].

Safety and effectiveness of VEMLIDY has not been established in pediatric patients with chronic HBV infection who are less than 6 years of age or weigh less than 25 kg.

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	June 11, 2025
Time period of search	November 10, 2016[†] to June 10, 2025
Search type	RxLogix Pediatric Focused Review Alert – DPV
Product terms	Product active ingredient: tenofovir alafenamide, tenofovir alafenamide fumarate
MedDRA search terms (Version 28.0)	All Preferred Terms
Other criteria	Case Seriousness: Serious Country Derived: USA

[*] See Appendix A for a description of the FAERS database.
[†] U.S. approval date for tenofovir alafenamide
Abbreviation: MedDRA=Medical Dictionary for Regulatory Activities

3 RESULTS

3.1 SELECTION OF U.S. SERIOUS PEDIATRIC CASES IN FAERS

Our FAERS search retrieved four U.S. serious[1] pediatric reports for patients less than 18 years old from November 10, 2016 to June 10, 2025.[2] We excluded all four reports from the case series as they described transplacental exposure.

After excluding reports as described above, 0 cases remained for discussion.

3.2 SUMMARY OF U.S. FATAL PEDIATRIC CASES (N=0)

[1] 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.
[2] Includes one pediatric report that was identified among reports not coded with an age.

There are no fatal pediatric adverse event cases for discussion.

3.3 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 tenofovir alafenamide in pediatric patients less than 18 years of age from November 10, 2016, to June 10, 2025, and identified four reports; however, all reports were excluded from further discussion as they described transplacental exposure.

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

5 CONCLUSION

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

6 REFERENCES

1. Vemlidy NDA 208464 Approval Letter. November 10, 2016. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2016/208464Orig1s000ltr.pdf
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3. Vemlidy NDA 208464/S-14 Supplement Approval Letter. October 17, 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2022/208464Orig1s014ltr.pdf
4. Vemlidy NDA 208464/S-16, NDA 208464/S-17 Supplement Approval Letter. March 27, 2024. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2024/208464Orig1s016,s017ltr.pdf

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.