Department of Health and Human Services
Public Health Service
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:	December 12, 2024
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Product Name:	Eraxis (anidulafungin) for injection, for intravenous use
Pediatric Labeling Approval Date:	September 22, 2020
Application Type/Number:	NDA 021632
Applicant:	Vicuron Holdings, LLC c/o Pfizer, Inc
TTT Record ID:	2024-11739

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EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Eraxis (anidulafungin) in pediatric patients less than 17 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 anidulafungin in pediatric patients.

Eraxis (anidulafungin) is an echinocandin antifungal that was initially approved in the U.S. on February 17, 2006, for the treatment of candidemia and other forms of *Candida* infections (intra-abdominal abscess and peritonitis) and esophageal candidiasis in adult patients. On September 22, 2020, the indication for the treatment of candidemia and other forms of *Candida* infections (intra-abdominal abscess and peritonitis) was expanded to include use in pediatric patients 1 month of age and older.

This pediatric postmarketing safety review was prompted by the pediatric labeling on September 22, 2020, that included the new pediatric indication.

DPV has not previously completed a pediatric postmarketing pharmacovigilance review for anidulafungin for the Pediatric Advisory Committee.

DPV reviewed all U.S. serious FAERS reports with anidulafungin in pediatric patients less than 17 years of age through November 17, 2024, and identified five reports; however, all reports were excluded from further discussion.

There were no new safety signals identified, no increased severity of any labeled adverse events, and no deaths directly associated with anidulafungin in pediatric patients less than 17 years of age.

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

1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Eraxis (anidulafungin) in pediatric patients less than 17 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 anidulafungin in pediatric patients.

1.1 PEDIATRIC REGULATORY HISTORY

Eraxis (anidulafungin) is an echinocandin antifungal that was initially approved in the U.S. on February 17, 2006, for the treatment of candidemia and other forms of *Candida* infections (intra-abdominal abscess and peritonitis) and esophageal candidiasis in adult patients.[1] On September 22, 2020, the indication for the treatment of candidemia and other forms of *Candida* infections (intra-abdominal abscess and peritonitis) was expanded to include use in pediatric patients 1 month of age and older.[2]

This pediatric postmarketing safety review was prompted by the pediatric labeling on September 22, 2020, that included the new pediatric indication.

DPV has not previously completed a pediatric postmarketing pharmacovigilance review for anidulafungin for the Pediatric Advisory Committee.

1.2 RELEVANT LABELED SAFETY INFORMATION[3]

The Eraxis (anidulafungin) labeling contains the following safety information excerpted from the Highlights of Prescribing Information and the *Pediatric Use* subsection. For additional anidulafungin labeling information, please refer to the full prescribing information.

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

- Known hypersensitivity to anidulafungin, any component of ERAXIS, or other echinocandins (4, 5.2)
- Known or suspected Hereditary Fructose Intolerance (HFI) (4, 5.4)

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

- Hepatic Effects: Risk of abnormal liver tests, hepatitis, hepatic failure; monitor hepatic function during therapy. (5.1, 13.2)
- Hypersensitivity: Anaphylaxis, including shock has been reported. Risk of infusion-related adverse reactions, possibly histamine-mediated, including rash, urticaria, flushing, pruritus, bronchospasm, dyspnea, and hypotension; to reduce occurrence, do not exceed a rate of infusion of 1.1 mg/minute. (2.4, 5.2)
- Risk of Neonatal Toxicity Associated with Polysorbates: ERAXIS contains polysorbate 80, an inactive ingredient. Thrombocytopenia, renal dysfunction, hepatomegaly, cholestasis, ascites, hypotension and metabolic acidosis haves been reported in low-birth weight infants receiving high doses of polysorbate. ERAXIS is not approved in pediatric patients younger than 1 month of age. (5.3, 8.4)
- Hereditary Fructose Intolerance (HFI): ERAXIS contains fructose. Risk of metabolic crisis with life-threatening hypoglycemia, hypophosphatemia, lactic acidosis, and hepatic failure. Obtain history of HFI symptoms in pediatric patients before ERAXIS administration. (5.4, 8.4)

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

Adults

- Candidemia and other forms of *Candida* infections: Most common adverse reactions (≥15%) are hypokalemia, nausea, diarrhea, vomiting, pyrexia, insomnia, hypotension. (6.1)
- Esophageal candidiasis: Most common adverse reactions (≥5%) are diarrhea, pyrexia, anemia, headache, vomiting, nausea, dyspepsia, oral candidiasis, and hypokalemia. (6.1)

Pediatric Patients (1 month and older)
Candidemia and other forms of *Candida* infections: Most common adverse reactions (≥ 5%): diarrhea, vomiting, pyrexia, abdominal pain, anemia, thrombocytopenia, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) increased, hypoglycemia, epistaxis, and rash. (6.1)

8.4 Pediatric Use

The safety and effectiveness of ERAXIS for the treatment of candidemia and the following *Candida* infections: intra-abdominal abscess and peritonitis, have been established in pediatric patients 1 month of age and older. Use of ERAXIS for this indication in this age group is supported by evidence from adequate and well-controlled studies in adults with additional pharmacokinetic, safety data in pediatric patients 1 month of age and older *[see Indications and Usage (1), Adverse Reactions (6.1), Clinical Pharmacology (12.3), and Clinical Studies (14.1)]*.

The safety and effectiveness of ERAXIS in patients younger than 1 month of age with candidemia/invasive candidiasis has not been established.

Candidemia/invasive candidiasis in pediatric patients younger than 1 month of age has a higher rate of central nervous system (CNS) and multi-organ dissemination than in older patients. In addition, in patients younger than 1 month of age ERAXIS carries a potential risk of life-threatening toxicity associated with high doses of polysorbate 80, an inactive ingredient in ERAXIS *[see Warnings and Precautions (5.3)]*.

The safety and effectiveness of ERAXIS in pediatric patients with esophageal candidiasis has not been established.

ERAXIS is contraindicated in adult and pediatric patients with HFI. Because a diagnosis of HFI may not yet be established in pediatric patients, obtain a careful history of HFI symptoms with fructose/sucrose exposure prior to administration of ERAXIS *[see Warnings and Precautions (5.4)]*.

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	November 18, 2024
Time period of search	All dates through November 17, 2024
Search type	RxLogix Pediatric Focused Review Alert – DPV
Product terms	Product Active Ingredient: anidulafungin
MedDRA search terms (Version 27.1)	All Preferred Terms
Other search terms†	Case Seriousness: Serious
* See Appendix A for a description of the FAERS database. † 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. Abbreviation: MedDRA=Medical Dictionary for Regulatory Activities	

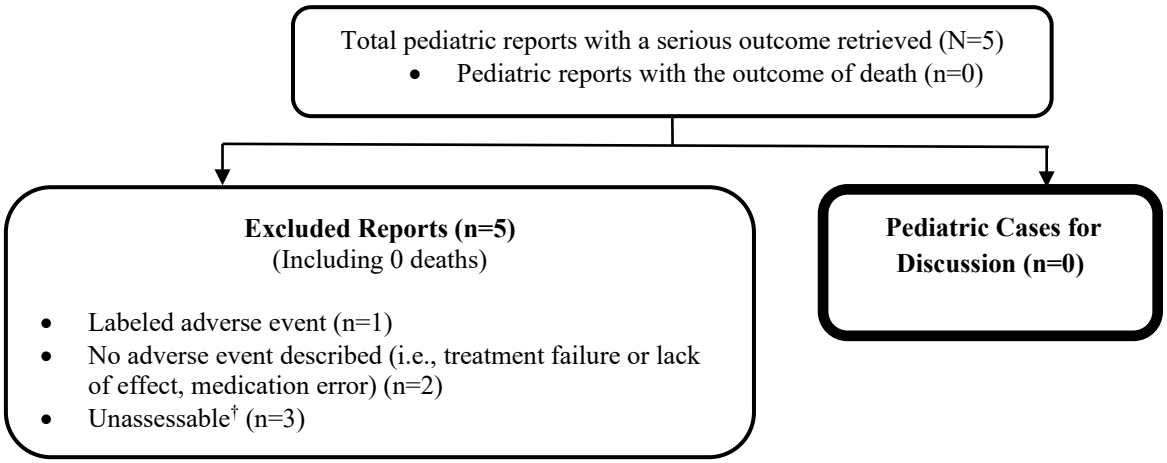
3 RESULTS

3.1 FAERS

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

Our FAERS search retrieved five U.S. serious pediatric reports for patients less than 17 years old through November 17, 2024. We reviewed all U.S. FAERS pediatric reports with a serious outcome. We excluded all five reports from the case series for the reasons listed in **Figure 1**. **Figure 1** presents the selection of cases for the pediatric case series.

Figure 1. Selection of U.S. Serious Pediatric Cases With Anidulafungin



* Labeled adverse event does not represent increased severity.
† Unassessable: The report cannot be assessed for causality because there is insufficient information reported (i.e., unknown time to event, concomitant medications and comorbidities, clinical course and outcome), the information is contradictory, or information provided in the report cannot be supplemented or verified.

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 anidulafungin in pediatric patients less than 17 years of age through November 17, 2024, and identified five reports; however, all reports were excluded from further discussion.

There were no new safety signals identified, no increased severity of any labeled adverse events, and no deaths directly associated with anidulafungin in pediatric patients less than 17 years of age.

5 CONCLUSION

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

6 REFERENCES

1. Eraxis (anidulafungin) for injection. [Prescribing information]. New York, NY; Pfizer, Inc.: February 2006.
2. Eraxis (anidulafungin) for injection, for intravenous use. [Prescribing information]. New York, NY; Pfizer, Inc.: September 2020.
3. Eraxis (anidulafungin) for injection, for intravenous use. [Prescribing information]. New York, NY; Pfizer, Inc.: October 2020.

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.