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:	January 8, 2025
Reviewers:	Debra Ryan, PharmD, MBA, Safety Evaluator Division of Pharmacovigilance I (DPV-I) Ivone Kim, MD, Medical Officer DPV-I
Team Leader:	Carmen Cheng, PharmD DPV-I
Division Director:	Monica Muñoz, PharmD, PhD, BCPS DPV-I
Product Name:	Eucrisa (crisaborole)
Pediatric Labeling Approval Dates:	March 23, 2020 (Supplement 10) April 3, 2023 (Supplement 12)
Application Type/Number:	NDA 207695
Applicant:	Anacor Pharmaceuticals, Inc.
TTT Record ID:	2024-12068

TABLE OF CONTENTS

EXECUTIVE SUMMARY

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

Eucrisa (crisaborole) ointment is a phosphodiesterase 4 inhibitor approved in the U.S. on December 14, 2016. Crisaborole is currently indicated for the topical treatment of mild to moderate atopic dermatitis in patients 3 months of age and older.

This review was stimulated by pediatric labeling on March 23, 2020, which extended the use of crisaborole for the topical treatment of mild to moderate atopic dermatitis in pediatric patients 3 months to less than 2 years old; and the pediatric labeling change on April 3, 2023, which changed the dosing regimen from applying twice daily to apply twice daily and consider reducing application to once daily, once clinical effect is achieved.

On February 7, 2019, the Office of Surveillance and Epidemiology (OSE) completed a review of postmarketing adverse event reports with a serious outcome for crisaborole in pediatric patients. OSE's evaluation did not identify any new safety concerns and recommended return to routine monitoring for adverse events with crisaborole. On March 28, 2019, OSE's evaluation was presented to the Pediatric Advisory Committee via webposting.

DPV reviewed all U.S. serious FAERS reports with crisaborole in pediatric patients less than 18 years of age from July 5, 2018, through November 17, 2024, and identified 45 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 crisaborole in pediatric patients less than 18 years of age.

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

1 INTRODUCTION

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

1.1 PEDIATRIC REGULATORY HISTORY[1]

Eucrisa (crisaborole) ointment is a phosphodiesterase 4 inhibitor approved in the U.S. on December 14, 2016. Crisaborole was initially approved for the topical treatment of mild to moderate atopic dermatitis in patients 2 years of age and older. This review was stimulated by pediatric labeling on March 23, 2020, which extended the use of crisaborole for the topical treatment of mild to moderate atopic dermatitis in pediatric patients 3 months to less than 2 years old; and the pediatric labeling change on April 3, 2023, which changed the dosing regimen from applying twice daily to apply twice daily and consider reducing application to once daily, once clinical effect is achieved.

On February 7, 2019, the Office of Surveillance and Epidemiology (OSE) completed a review of postmarketing adverse event reports with a serious outcome for crisaborole in pediatric patients. OSE's evaluation did not identify any new safety concerns and recommended return to routine monitoring for adverse events with crisaborole. On March 28, 2019, OSE's evaluation was presented to the Pediatric Advisory Committee via webposting.[2]

1.2 RELEVANT LABELED SAFETY INFORMATION[1]

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

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

- Known hypersensitivity to crisaborole or any component of the formulation.

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

- Hypersensitivity reactions: If signs and symptoms of hypersensitivity occur, discontinue EUCRISA immediately and initiate appropriate therapy.

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

- Most common adverse reaction occurring in ≥1% in subjects is application site pain.

----------USE IN SPECIFIC POPULATIONS----------

8.4 Pediatric Use

The safety and effectiveness of EUCRISA have been established in pediatric patients ages 3 months and older for topical treatment of mild to moderate atopic dermatitis. Use of EUCRISA administered twice daily in this age group is supported by data from two 28-day adequate, vehicle-controlled safety and efficacy trials (1,313 pediatric subjects ages 2 years to 17 years of whom 874 received EUCRISA), a 28-day open-label, safety and pharmacokinetics (PK) trial (137 subjects ages 3 months to less than 2 years who received EUCRISA), and another trial with an open-label period of up to 8 weeks (327 pediatric subjects ages 5 months to less than 18 years who received EUCRISA).

2 METHODS AND MATERIALS

2.1 FAERS SEARCH STRATEGY

DPV searched the FAERS database with the strategy described in Table I.

Table I. FAERS Search Strategy*	
Date of search	November 18, 2024
Time period of search	July 5, 2018† - November 17, 2024
Search type	RxLogix Pediatric Focused Review Alert - DPV
Product term	Product Active Ingredient: crisaborole
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. † The FAERS search period for the most recently completed DPV pediatric postmarketing pharmacovigilance review for crisaborole ended on July 4, 2018. ‡ 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	

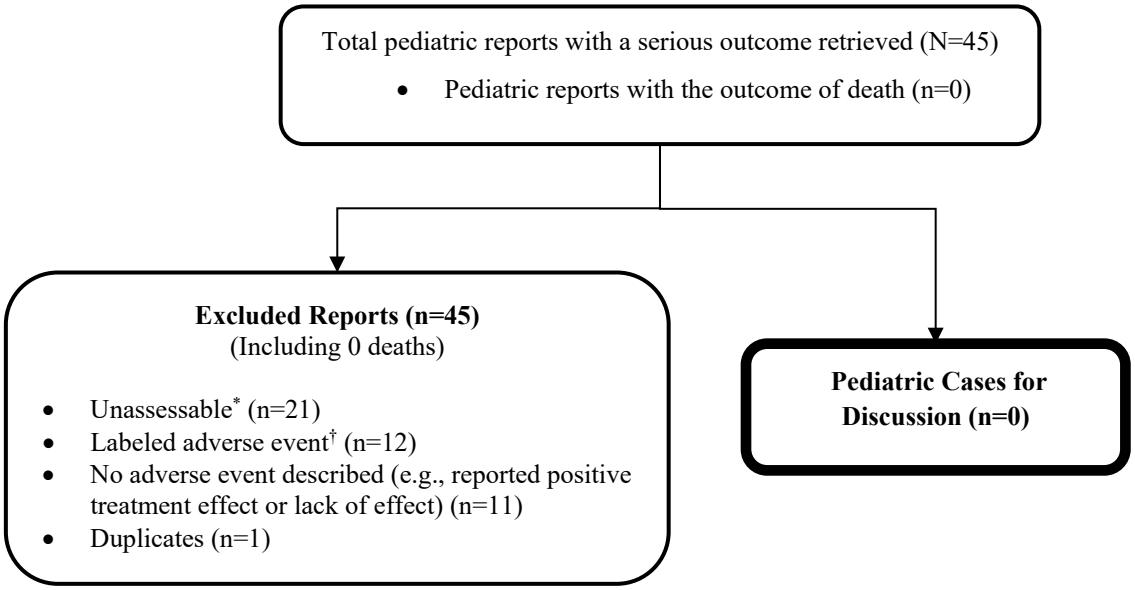
3 RESULTS

3.1 FAERS

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

Our FAERS search retrieved 45 U.S. serious pediatric reports for patients less than 18 years old from July 5, 2018, through November 17, 2024. We reviewed all U.S. FAERS pediatric reports with a serious outcome. We excluded all 45 reports from the case series for the reasons listed in Figure 1.

Figure 1. Selection of U.S. Serious Pediatric Cases with Crisaborole



* 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.
† Labeled adverse event does not represent increased severity.

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 crisaborole in pediatric patients less than 18 years of age from July 5, 2018, through November 17, 2024, and identified 45 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 crisaborole in pediatric patients less than 18 years of age.

5 CONCLUSION

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

6 REFERENCES

1. Eucrisa (crisaborole) [package insert]. New York, NY. Anacor Pharmaceuticals, Inc. Revised April 2023.

2. Eucrisa (crisaborole) ointment 2%. Pediatric Postmarketing Pharmacovigilance and Drug Utilization Review. February 7, 2019. Accessed: December 23, 2024. Available at: https://www.fda.gov/media/123634/download

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.