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:	October 24, 2023
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Product Name:	Jublia (efinaconazole) topical solution
Pediatric Labeling Approval Date:	April 26, 2020
Application Type/Number:	NDA 203567
Applicant:	Bausch Health Americas, Inc.
TTT Record ID:	2023-5804

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EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Jublia (efinaconazole) topical solution 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 serious unlabeled adverse events associated with efinaconazole in pediatric patients.

Jublia (efinaconazole) topical solution is an azole antifungal that was initially approved in the U.S. on June 6, 2014. Jublia is currently indicated for the topical treatment of onychomycosis of the toenail due to *Trichophyton rubrum* and *Trichophyton mentagrophytes*.

This pediatric postmarketing safety review was prompted by pediatric labeling on April 26, 2020, which expanded the indication for use in pediatric patients aged 6 years and older. Safety and effectiveness have not been established in patients younger than 6 years. A pediatric safety review for efinaconazole has not been previously presented to the Pediatric Advisory Committee.

DPV searched FAERS for all serious reports with efinaconazole in pediatric patients less than 17 years of age from June 6, 2014 – July 31, 2023, and did not identify any reports.

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

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

1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Julia (efinaconazole) topical solution 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 serious unlabeled adverse events associated with efinaconazole in pediatric patients.

1.1 PEDIATRIC REGULATORY HISTORY[1]

Julia (efinaconazole) topical solution is an azole antifungal that was initially approved in the U.S. on June 6, 2014. Julia is currently indicated for the topical treatment of onychomycosis of the toenail due to *Trichophyton rubrum* and *Trichophyton mentaghrophytes*.[1]

This pediatric postmarketing safety review was prompted by pediatric labeling on April 26, 2020, which expanded the indication for use in pediatric patients aged 6 years and older.[1] Safety and effectiveness has not been established in patients younger than 6 years. A pediatric safety review for efinaconazole has not been previously presented to the Pediatric Advisory Committee.

1.2 RELEVANT LABELED SAFETY INFORMATION

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

---------- CONTRAINDICATIONS ----------
None. (4)

---------- ADVERSE REACTIONS ----------
The most common adverse reactions (incidence >1%) were ingrown toenails, application site dermatitis, application site vesicles, and application site pain. (6.1)

8.4 Pediatric Use
The safety and effectiveness of JUBLIA were established in patients 6 years and older. Use of JUBLIA in these age groups is supported by evidence from well-controlled trials in adults with additional data from an open-label safety study in 60 pediatric subjects ages 6 to 17 (including a pharmacokinetic study in 17 subjects 12 years to less than 17 years old) [see Clinical Pharmacology (12.3)]. Safety and effectiveness of JUBLIA in pediatric subjects under 6 years of age 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	August 1, 2023
Time period of search	June 6, 2014† - July 31, 2023
Search type	RxLogix Post-Market Cases
Product terms	Product Active Ingredient: Efinaconazole
MedDRA search terms (Version 26.0)	All Preferred Terms

* See Appendix A for a description of the FAERS database.
† Jublia U.S. approval date
Abbreviations: MedDRA=Medical Dictionary for Regulatory Activities

3 RESULTS

3.1 FAERS

3.1.1 Total Number of FAERS Reports by Age

Table 2 presents the number of adult and pediatric FAERS reports from June 6, 2014 - July 31, 2023, with efinaconazole.

Table 2. Total Adult and Pediatric FAERS Reports* Received by FDA From June 6, 2014 – July 31, 2023, With Efinaconazole			
	All Reports (U.S.)	**Serious† (U.S.)**	**Death (U.S.)**
Adults (≥ 17 years)	583 (487)	137 (47)	15 (2)
Pediatrics (0 - < 17 years)	6 (6)	0 (0)	0 (0)

* May include duplicates and transplacental exposures, and have not been assessed for causality
† 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.

3.1.2 Selection of Serious Pediatric Cases in FAERS

Our FAERS search retrieved zero serious pediatric reports from June 6, 2014 – July 31, 2023.

3.1.3 Summary of Fatal Pediatric Cases (N=0)

There are no fatal pediatric adverse event cases for discussion.

3.1.4 Summary of Serious Non-Fatal Pediatric Cases (N=0)

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

4 DISCUSSION

DPV searched FAERS for all serious reports with efinaconazole in pediatric patients less than 17 years of age from June 6, 2014 – July 31, 2023, and did not identify any reports.

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

5 CONCLUSION

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

6 REFERENCES

1. Julia (efinaconazole) topical solution [Prescribing information]. Bridgewater, NJ; Bausch Health U.S., LLC.: March, 2023.

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.

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