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:	Arazlo (tazarotene) lotion
Pediatric Labeling Approval Date:	December 18, 2019
Application Type/Number:	NDA 211882
Applicant:	Bausch Health U.S., LLC
TTT Record ID:	2023-5803

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EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Arazlo (tazarotene) lotion 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 tazarotene in pediatric patients.

Arazlo (tazarotene) lotion is a retinoid that was initially approved in the U.S. on December 18, 2019. Arazlo is currently indicated for the topical treatment of acne vulgaris in patients 9 years of age and older.

This pediatric postmarketing safety review was prompted by pediatric labeling at FDA approval on December 18, 2019, that included an indication for pediatric patients aged 9 years and older. Safety and effectiveness of Arazlo in pediatric patients younger than 9 years old have not been established. A pediatric safety review for tazarotene has not been previously presented to the Pediatric Advisory Committee.

DPV reviewed a singular serious FAERS report with tazarotene in pediatric patients less than 17 years of age from December 18, 2019 – July 27, 2023; however, the report was excluded from further discussion as it did not report an adverse event.

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

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

1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Arazlo (tazarotene) lotion 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 tazarotene in pediatric patients.

1.1 PEDIATRIC REGULATORY HISTORY

Arazlo (tazarotene) lotion is a retinoid that was initially approved in the U.S. on December 18, 2019. Arazlo is currently indicated for the topical treatment of acne vulgaris in patients 9 years of age and older.[1]

This pediatric postmarketing safety review was prompted by pediatric labeling at initial FDA approval on December 18, 2019, which included an indication for pediatric patients. Safety and effectiveness for Arazlo in patients aged 9 years and older is based on evidence from two clinical trials and an open-label pharmacokinetic study.[1] Safety and effectiveness of Arazlo in pediatric patients younger than 9 years old have not been established.

A pediatric safety review for tazarotene has not previously been presented to the Pediatric Advisory Committee.

1.2 RELEVANT LABELED SAFETY INFORMATION

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

---------- CONTRAINDICATIONS ----------
ARAZLO is contraindicated in pregnancy. (4, 8.1)

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

- Embryofetal Toxicity: May cause fetal harm when administered during pregnancy. Patients of childbearing potential should have a negative pregnancy test within 2 weeks prior to initiating treatment and use effective contraception during treatment. (5.1)
- Skin Irritation: Pain, dryness, exfoliation, erythema, and pruritus may occur with use of ARAZLO. Avoid application to eczematous or sunburned skin. (5.2)
- Photosensitivity and Risk for Sunburn: Minimize exposure to sunlight and sunlamps. Use sunscreen and protective clothing when sun exposure cannot be avoided. Administer with caution if the patient is also taking drugs known to be photosensitizers. (5.3)

---------- ADVERSE REACTIONS ----------
The most common adverse reactions (occurring in ≥1% of the ARAZLO group and greater than the vehicle group) were application site reactions; pain, dryness, exfoliation, erythema and pruritus. (6.1)

8.4 Pediatric
Use Safety and effectiveness of ARAZLO for the topical treatment of acne vulgaris have been established in pediatric patients age 9 years and older based on evidence from two multicenter, randomized, double-blind, parallel-group, vehicle-controlled, 12-week clinical trials and an open-label pharmacokinetic study. A total of 300 pediatric subjects aged 9 to less than 17 years received ARAZLO in the clinical studies [see Clinical Pharmacology (12.3) and Clinical Studies (14)].

The safety and effectiveness of ARAZLO in pediatric patients below the age of 9 years 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	July 28, 2023
Time period of search	December 18, 2019† - July 27, 2023
Search type	RxLogix Post-Market Cases
Product terms	Product Active Ingredient: Tazarotene
MedDRA search terms (Version 26.0)	All Preferred Terms
* See Appendix A for a description of the FAERS database. † Approval date for Arazlo 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 December 18, 2019 – July 27, 2023, with tazarotene.

Table 2. Total Adult and Pediatric FAERS Reports* Received by FDA From December 18, 2019 – July 27, 2023, With Tazarotene			
	All Reports (U.S.)	**Serious† (U.S.)**	**Death (U.S.)**
Adults (≥ 17 years)	46 (43)	11 (9)	0 (0)
Pediatrics (0 - < 17 years)	7 (7)	1 (1)	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 one serious pediatric report from December 18, 2019 – July 27, 2023. We reviewed the singular FAERS pediatric report with a serious outcome. We excluded the report from the case series as it did not describe an adverse event.

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 reviewed a singular serious FAERS report with tazarotene in pediatric patients less than 17 years of age from December 18, 2019 – July 27, 2023; however, the report was excluded from further discussion.

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

5 CONCLUSION

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

6 REFERENCES

1. Arazlo (tazarotene) lotion, for topical use. [Prescribing information]. Bridgewater, NJ: Bausch Health US, LLC; December, 2019.

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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