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:	Vectical (calcitriol) ointment
Pediatric Labeling Approval Date:	July 17, 2020
Application Type/Number:	NDA 022087
Applicant:	Galderma Laboratories, L.P.
TTT Record ID:	2023-5912

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EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Vectical (calcitriol) ointment 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 serious unlabeled adverse events associated with Vectical in pediatric patients.

Vectical (calcitriol) ointment is a vitamin D analog initially approved in the U.S. on January 23, 2009. Vectical ointment is currently indicated for the topical treatment of mild to moderate plaque psoriasis in adult and pediatric patients aged 2 years and older. This pediatric postmarketing safety review was prompted by pediatric labeling on July 17, 2020, that extended the indication to include use in pediatric patients aged 2-17 years. The safety and effectiveness of Vectical have not been established in patients younger than 2 years old. A pediatric safety review for Vectical has not previously been presented to the Pediatric Advisory Committee.

DPV searched FAERS for all serious reports with Vectical in pediatric patients less than 18 years of age from January 23, 2009 – August 8, 2023, and identified one report; however, this 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 Vectical in pediatric patients less than 18 years of age.

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

1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Vectical (calcitriol) ointment 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 serious unlabeled adverse events associated with Vectical in pediatric patients.

1.1 PEDIATRIC REGULATORY HISTORY

Vectical (calcitriol) ointment is a vitamin D analog initially approved in the U.S. on January 23, 2009. Vectical ointment is currently indicated for the topical treatment of mild to moderate plaque psoriasis in adult and pediatric patients aged 2 years and older.[1]

This pediatric postmarketing safety review was prompted by pediatric labeling on July 17, 2020, that extended the indication to include use in pediatric patients aged 2-17 years. The safety and effectiveness of Vectical have not been established in patients younger than 2 years old.[1]

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

1.2 RELEVANT LABELED SAFETY INFORMATION

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

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

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

- Effects on Calcium metabolism: Risk of hypercalcemia. If aberrations in parameters of calcium metabolism are noted discontinue VECTICAL Ointment until these normalize. Increased absorption may occur with occlusive use. (5.1)
- VECTICAL Ointment should be used with caution in patients receiving medications known to increase the serum calcium level, such as thiazide diuretics, and in patients receiving calcium supplements or high doses of vitamin D. (5.1)

----------ADVERSE REACTIONS----------
Most common adverse reactions (incidence >3%) are hypercalcemia, hypercalciuria, and skin discomfort. (6.1).

8.4 Pediatric Use
The safety and effectiveness of VECTICAL Ointment have been established in pediatric patients age 2 years and older for topical treatment of mild to moderate psoriasis. Use of VECTICAL Ointment in this age group is supported by two adequate and well-controlled 8-week trials and an open label trial in adult subjects, and additional data from trials conducted in pediatric subjects 2 to 17 years of age including;

- a vehicle controlled 8-week trial in 19 subjects 2 to 12 years of age with mild to moderate plaque psoriasis
- an open-label 8-week safety and pharmacokinetics (PK) trial in 25 subjects 12 to 17 years of age

- an open-label 14-day safety and PK trial in 18 subjects 2 to 12 years of age; and
- an open-label 26-week safety and PK trial in 54 subjects 2 to 17 years of age.

Data from 63 subjects ages 2 to 12 years, and 42 subjects ages 13 to 17 years showed no significant effects on indices of calcium metabolism. The systemic exposure of calcitriol in the pediatric subjects was generally comparable to the endogenous levels observed at baseline. No new safety signals were identified in subjects 2 to 17 years [see Clinical Studies (14), Clinical Pharmacology (12.3) and Adverse Reactions (6.1)].

The safety and effectiveness of VECTICAL Ointment in pediatric subjects below the age of 2 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	August 9, 2023
Time period of search	January 23, 2009† - August 8, 2023
Search type	Drug Safety Analytics Dashboard (DSAD) Quick Query
Product terms	Product Name: Vectical NDA: 022087
MedDRA search terms (Version 26.0)	All Preferred Terms
* See Appendix A for a description of the FAERS database. † Vectical U.S. approval date. Abbreviations: MedDRA=Medical Dictionary for Regulatory Activities, NDA=New Drug Application	

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 January 23, 2009 – August 8, 2023, with Vectical.

Table 2. Total Adult and Pediatric FAERS Reports* Received by FDA From January 23, 2009 – August 8, 2023, With Vectical			
	All Reports (U.S.)	**Serious† (U.S.)**	**Death (U.S.)**
Adults (≥ 18 years)	32 (2)	13 (3)	0 (0)
Pediatrics (0 - < 18 years)	2 (1)	1 (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 one serious pediatric report from January 23, 2009 – August 8, 2023. We reviewed the singular pediatric report with a serious outcome and excluded it from further discussion as it described a labeled adverse event with Vectical. The labeled adverse event did not represent increased severity or frequency.

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 Vectical in pediatric patients less than 18 years of age from January 23, 2009 – August 8, 2023, and identified one report; however, this 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 Vectical in pediatric patients less than 18 years of age.

5 CONCLUSION

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

6 REFERENCES

1. Vectical (calcitriol) ointment, for topical use [Prescribing information]. Fort Worth, Texas; Galderma Laboratories, L.P.: July, 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.

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