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Office of Surveillance and Epidemiology
Office of Pharmacovigilance and Epidemiology

Pediatric Postmarketing Pharmacovigilance Review

Date:	August 31, 2023
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Product Name:	Sorilux (calcipotriene) foam
Pediatric Labeling Approval Dates:	May 6, 2019 November 5, 2019
Application Type/Number:	NDA 022563
Applicant:	Mayne Pharma, LLC
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TABLE OF CONTENTS

Executive Summary....1
1 Introduction....2
1.1 Pediatric Regulatory History....2
1.2 Relevant Labeled Safety Information....2
2 Methods and Materials....3
2.1 FAERS Search Strategy....3
3 Results....3
3.1 FAERS....3
3.1.1 Total Number of FAERS Reports by Age....3
3.1.2 Selection of Serious Pediatric Cases in FAERS....4
3.1.3 Summary of U.S. Fatal Pediatric Cases (N=0)....4
3.1.4 Summary of U.S. Serious Non-Fatal Pediatric Cases (N=0)....4
4 Discussion....4
5 Conclusion....4
6 References....4
7 Appendices....5
7.1 Appendix A. FDA Adverse Event Reporting System (FAERS)....5

EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Sorilux (calcipotriene) 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 Sorilux in pediatric patients.

Sorilux is a vitamin D analog initially approved in the United States (U.S.) on October 6, 2010. Sorilux is available as a foam, and it is currently indicated for the topical treatment of plaque psoriasis of the scalp and body in adults and pediatric patients 4 years of age and older. This pediatric postmarketing pharmacovigilance review was prompted by pediatric labeling changes on May 6, 2019, and November 5, 2019, that expanded indications for use in patients aged 12 years and up, and 4 years and up, respectively.

DPV reviewed all serious FAERS reports with Sorilux in pediatric patients less than 17 years of age from October 6, 2010 – July 10, 2023 (n=4). All four reports were excluded from further discussion after hands-on evaluation.

There were no new safety signals identified, no increased severity or frequency of any labeled adverse events, and no deaths directly associated with Sorilux in pediatric patients less than 17 years of age. DPV will continue routine pharmacovigilance monitoring for Sorilux.

1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Sorilux (calcipotriene) 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 Sorilux in pediatric patients.

1.1 PEDIATRIC REGULATORY HISTORY[1]

Sorilux is a vitamin D analog initially approved in the United States (U.S.) on October 6, 2010. Sorilux is available as a foam, and it is currently indicated for the topical treatment of plaque psoriasis of the scalp and body in adults and pediatric patients 4 years of age and older.

This pediatric postmarketing safety review was prompted by the following pediatric labeling changes:

> May 6, 2019: Labeling change to reflect the expanded indication to include pediatric patients aged 12 years and older.
>
> November 5, 2019: Labeling change to reflect the expanded indication to include pediatric patients aged 4 years and older.

Support for use of Sorilux in pediatric patients aged 4 years and older derived from two adequate and well controlled 8-week trials in adults and adolescents 12 years and older, with additional data from a 15-day open-label safety and pharmacokinetics (PK) study conducted in 19 subjects aged 12-16 years of age; and an 8-week open-label safety and PK study in 36 subjects aged 4-11 years with psoriasis. Data from 19 subjects aged 12-16 years and 18 subjects aged 5-11 years showed no significant effects on indices of calcium metabolism. Systemic concentrations of calcipotriene were not quantifiable in two studies in subjects aged 7-16 years. The safety and effectiveness of Sorilux in pediatric patients younger than 4 years of age have not been established. Sorilux has not been previously presented before the Pediatric Advisory Committee.

1.2 RELEVANT LABELED SAFETY INFORMATION[1]

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

> ----------CONTRAINDICATION----------
> • Do not use in patients with known hypercalcemia. (4)
>
> ----------WARNINGS AND PRECAUTIONS----------
> • Flammability: Contents are flammable. Instruct the patient the avoid fire, flame, and smoking during and immediately following application. (5.1)
> • Effects on Calcium Metabolism: If elevation of serum calcium occurs, instruct patients to discontinue treatment until normal calcium levels are restored. (5.2)
>
> ----------ADVERSE REACTIONS----------

Adverse reactions reported in ≥ 1% of subjects treated with SORILUX Foam and at a higher incidence than subjects treated with vehicle were application site erythema and application site pain. (6.1)

8.4 Pediatric Use
The safety and effectiveness of SORILUX Foam have been established in pediatric patients age 4 years and older for topical treatment of plaque psoriasis of the scalp and body.

Use of SORILUX Foam in this age group is supported by two adequate and well controlled 8-week trials in adults and adolescents 12 years of age and older, with additional data from a 15-day open-label safety and pharmacokinetics (PK) study conducted in 19 subjects 12 to less than 17 years of age; and an 8-week open-label safety and PK study in 36 subjects 4 to 11 years of age with psoriasis. Data from 19 subjects aged 12 to less than 17 years and 18 subjects aged 5 to 11 years showed no significant effects on indices of calcium metabolism. Systemic concentrations of calcipotriene were not quantifiable in the two studies in subjects aged 7 years to less than 17 years. [see Clinical Studies (14), Clinical Pharmacology (12.2, 12.3) and Adverse Reactions (6.1)].

The safety and effectiveness of SORILUX Foam in pediatric patients less than 4 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	July 11, 2023
Time period of search	October 6, 2010† - July 10, 2023
Search type	RxLogix Post-Market Cases
Product terms	Product active ingredient: calcipotriene
MedDRA search terms (Version 26.0)	All Preferred Terms
* See Appendix A for a description of the FAERS database. † Sorilux 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

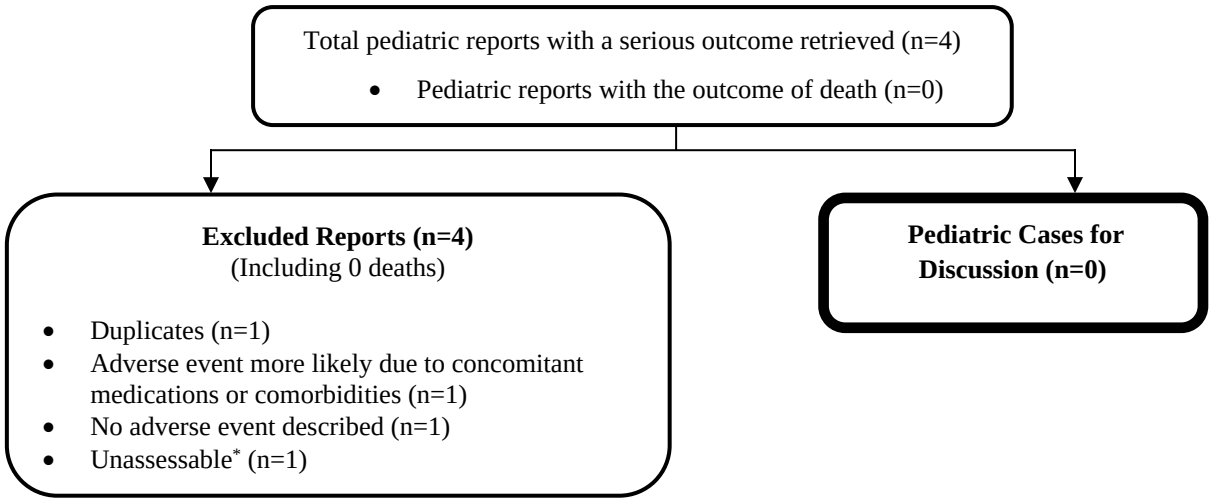
Table 2 presents the number of adult and pediatric FAERS reports from October 6, 2010 – July 10, 2023, with Sorilux.

Table 2. Total Adult and Pediatric FAERS Reports* Received by FDA From October 6, 2010 – July 10, 2023, With Sorilux			
	All reports (U.S.)	**Serious† (U.S.)**	**Death (U.S.)**
Adults (≥ 17 years)	296 (146)	210 (74)	0 (0)
Pediatrics (0 - <17 years)	8 (4)	4 (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 4 serious pediatric reports from October 6, 2010 – July 10, 2023, with Sorilux. We reviewed all FAERS pediatric reports with a serious outcome and excluded all 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 Serious Pediatric Cases with Sorilux



* 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.

3.1.3 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 all serious FAERS reports with Sorilux in pediatric patients less than 17 years of age from October 6, 2010 – July 10, 2023, and 4 reports were identified; however, all reports were 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 Sorilux in pediatric patients less than 17 years of age.

5 CONCLUSION

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

6 REFERENCES

1. Sorilux (calcipotriene) foam, for topical use [package insert]. Greenville, NC: Mayne Pharma, LLC; November, 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 (MedDRA) terminology. The suspect products are coded to valid tradenames or active ingredients in the FAERS Product Dictionary (FPD). 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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