Department of Health and Human Services
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Office of Surveillance and Epidemiology
Office of Pharmacovigilance and Epidemiology

Pediatric Postmarketing Pharmacovigilance Review

Date:	June 10, 2024
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Product Name:	Topicort (desoximetasone) topical spray
Pediatric Labeling Approval Date:	October 7, 2021
Application Type/Number:	NDA 204141
Applicant:	Taro Pharmaceuticals
TTT Record ID:	2024-9447

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EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Topicort (desoximetasone) topical spray 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 United States (U.S.) serious unlabeled adverse events associated with desoximetasone in pediatric patients.

Topicort (desoximetasone) topical spray is a corticosteroid first approved by FDA on April 11, 2013, and it is currently indicated for the treatment of plaque psoriasis in patients aged 18 years or older.

On October 7, 2021, the labeling for desoximetasone topical spray was updated to reflect findings from an open-label, sequential cohort, safety trial evaluating the potential for hypothalamic-pituitary-adrenal (HPA) axis suppression with desoximetasone topical spray. Findings from the study failed to establish safety and effectiveness for desoximetasone topical spray in pediatric patients for the treatment of plaque psoriasis. Desoximetasone topical spray is not indicated for use in patients younger than 18 years old.

This pediatric postmarketing safety review was prompted by the pediatric labeling on October 7, 2021. DPV has not previously performed a pediatric postmarketing pharmacovigilance review for desoximetasone for the Pediatric Advisory Committee.

DPV reviewed all serious FAERS reports with desoximetasone in pediatric patients less than 18 years of age through May 2, 2024. DPV identified 118 serious 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 desoximetasone in pediatric patients less than 18 years of age.

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

1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Topicort (desoximetasone) topical spray 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 United States (U.S.) serious unlabeled adverse events associated with desoximetasone in pediatric patients.

1.1 PEDIATRIC REGULATORY HISTORY

Topicort (desoximetasone) topical spray is a corticosteroid first approved by FDA on April 11, 2013, and it is currently indicated for the treatment of plaque psoriasis in patients aged 18 years or older.[1]

Desoximetasone is also available in topical cream, gel, and ointment formulations. **Appendix A** contains a listing of desoximetasone products currently marketed in the United States.

On October 7, 2021, the labeling for desoximetasone topical spray was updated to reflect findings from an open-label, sequential cohort, safety trial evaluating the potential for hypothalamic-pituitary-adrenal (HPA) axis suppression with desoximetasone topical spray. Findings from the study failed to establish safety and effectiveness for desoximetasone topical spray in pediatric patients for the treatment of plaque psoriasis. Desoximetasone topical spray is not indicated for use in patients younger than 18 years old.[2]

This pediatric postmarketing safety review was prompted by the pediatric labeling on October 7, 2021. DPV has not previously performed a pediatric postmarketing pharmacovigilance review for desoximetasone for the Pediatric Advisory Committee.

1.2 RELEVANT LABELED SAFETY INFORMATION

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

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

- *Effect on Endocrine System:* Topicort® Topical Spray can produce reversible HPA axis suppression with the potential for glucocorticosteroid insufficiency during or after treatment. (5.1)
    - Cushing's syndrome, hyperglycemia, and unmasking of latent diabetes mellitus can result from systemic absorption of topical corticosteroids. (5.1)
    - Because of the potential for systemic absorption, use of topical corticosteroids may require that patients be periodically evaluated for HPA axis suppression. (5.1)
    - Modify use if HPA axis suppression develops. (5.1)
    - High potency corticosteroids, large treatment surface areas, prolonged use, use of occlusive dressings, altered skin barrier, liver failure and young age may predispose patients to HPA axis suppression. (5.1)
    - Pediatric patients may be more susceptible to systemic toxicity when treated with topical corticosteroids. Safety and effectiveness have not been established in pediatric patients and use in pediatric patients is not recommended. (5.1, 8.4)
- *Ophthalmic Adverse Reactions:* Topical corticosteroid products may increase the risk of cataracts and glaucoma. If visual symptoms occur, consider referral to an ophthalmologist. (5.3)

- *Flammability:* Topicort Topical Spray is flammable; keep away from heat or flame. (5.6)

----------ADVERSE REACTIONS----------
The most common adverse reactions (≥ 1%) are application site dryness, application site irritation and application site pruritus. (6.1)

8.4 Pediatric Use

The safety and effectiveness of Topicort Topical Spray have not been established in pediatric patients for the treatment of plaque psoriasis. Topicort Topical Spray is not recommended for use in patients less than 18 years of age due to the high incidence of HPA axis suppression observed [see Warnings and Precautions (5.1)].

Hypothalamic-Pituitary Adrenal (HPA) Axis Suppression
The HPA axis suppression potential of Topicort Topical Spray was assessed in an open-label, sequential cohort, safety trial in 129 subjects 2 years to less than 18 years of age with moderate to severe plaque psoriasis defined as a Physician Global Assessment (PGA) score of ≥3 with involvement of at least 10% of their body surface area (excluding the face and scalp). In total, 100 pediatric subjects were evaluated for HPA axis function via cosyntropin stimulation testing at baseline and following 4 weeks of twice daily application of Topicort Topical Spray. Overall, 36% of pediatric subjects 2 years to less than 18 years of age demonstrated HPA axis suppression defined as a serum cortisol level ≤ 18 mcg/dL 30-minutes post cosyntropin stimulation. The proportion of subjects demonstrating HPA axis suppression was 35.0% in Cohort 1 (12 years to less than 18 years of age) and 43.3% in Cohort 2 (6 years to less than 12 years of age). Trial enrollment in the youngest cohort (2 years to less than 6 years of age) was discontinued early due to high incidence of HPA axis suppression observed in the two oldest cohorts (6 years to less than 18 years of age) [see Clinical Pharmacology (12.2)].

Because of a higher ratio of skin surface area to body mass, pediatric patients are at a greater risk than adults of HPA axis suppression and Cushing's syndrome when they are treated with topical corticosteroids. They are therefore at greater risk of adrenal insufficiency during and/or after withdrawal of treatment. Adverse reactions including striae have been reported with inappropriate use of topical corticosteroids in infants and children.

HPA axis suppression, Cushing's syndrome, linear growth retardation, delayed weight gain, and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children include low plasma cortisol levels and absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema.

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	May 3, 2024
Time period of search	All dates through May 2, 2024
Search type	RxLogix Pediatric Focused Review Alert – DPV
Product terms	Product active ingredient: desoximetasone
MedDRA search terms (Version 26.1)	All Preferred Terms
* See Appendix B for a description of the FAERS database. 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 through May 2, 2024, with desoximetasone.

Table 2. Total Adult and Pediatric FAERS Reports* Received by FDA Through May 2, 2024, With Desoximetasone

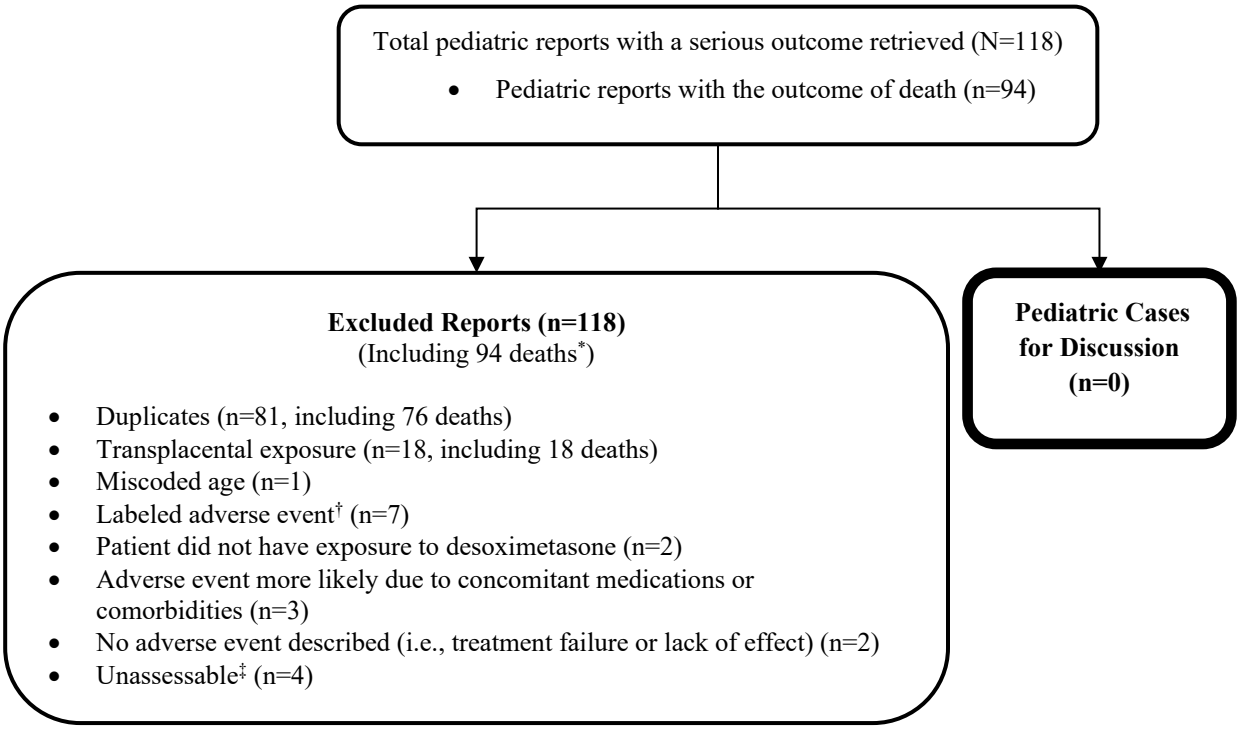
	All Reports (U.S.)	Serious† (U.S.)	Death (U.S.)
Adults (≥ 18 years)	3,128 (208)	3,023 (106)	593 (19)
Pediatrics (0 - < 18 years)	125‡ (24)	118‡ (17)	94‡ (0)

* 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.
‡ See Figure 1. DPV identified an additional 94 reports of pediatric deaths among reports not reporting an age. These reports are reflected in the counts of pediatric reports.

3.1.2 Selection of Serious Pediatric Cases in FAERS

Our FAERS search retrieved 118 serious pediatric reports through May 2, 2024 with desoximetasone. We reviewed all FAERS pediatric reports with a serious outcome. We excluded all 118 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 Desoximetasone



* Of the excluded FAERS reports, 94 described fatal outcomes. After accounting for duplicate repots (n=76), DPV identified 18 unique cases describing a fatal outcome. All 18 cases described neonatal or fetal death after prenatal exposure to desoximetasone. All cases described prenatal exposure to multiple

medications, suggested complex maternal comorbid conditions, and lacked any clinical detail about the patients' prenatal and postnatal course. Therefore, DPV was unable to attribute any of the deaths to desoximetasone.

† Labeled adverse event does not represent increased severity or frequency.

‡ 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 desoximetasone in pediatric patients less than 18 years of age through May 2, 2024. DPV identified 118 serious 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 desoximetasone in pediatric patients less than 18 years of age.

5 CONCLUSION

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

6 REFERENCES

1. Topicort (desoximetasone) topical spray. [Prescribing information]. Hawthorn, NY; Taro Pharmaceuticals U.S.A.: April 2013.
2. Topicort (desoximetasone) topical spray. [Prescribing information]. Hawthorn, NY; Taro Pharmaceuticals U.S.A.: October 2021.

7 APPENDICES

7.1 APPENDIX A. CURRENTLY MARKETED DESOXIMETASONE PRODUCTS

Current Desoximetasone Products Marketed in the United States					
Proprietary Name	**Active Ingredient**	**Application Number**	**Strength**	**Dosage Form**	**Indication**
Topicort	Desoximetasone	NDA 018594	0.05%	Ointment	Relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses
--	Desoximetasone	ANDA 208044, 209973			
Topicort	Desoximetasone	ANDA 018594			
--	Desoximetasone	ANDA 077770, 204965, 201005, 078657, 202838, 208104, 206792, 204272, 205206	0.25%		
Topicort	Desoximetasone	NDA 204141	0.25%	Spray	Treatment of plaque psoriasis in patients 18 years or age or older
--	Desoximetasone	ANDA 208124, 206441,			
Topicort	Desoximetasone	ANDA 074904	0.05%	Gel	Relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses
--	Desoximetasone	ANDA 077552, 090727, 204675			
Topicort	Desoximetasone	ANDA 073210	0.05%	Cream	Relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses
--	Desoximetasone	ANDA 208163, 210980,			
--	Desoximetasone	ANDA 076510, 205082, 078369, 208164, 205594, 205620, 073193	0.25%		
Abbreviations: ANDA=Abbreviated New Drug Application, NDA=New Drug Application					

7.2 APPENDIX B. 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.