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:	May 7, 2024
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Product Name:	Xaciato (clindamycin phosphate) vaginal gel
Pediatric Labeling Approval Date:	December 7, 2021
Application Type/Number:	NDA 215650
Applicant:	Organon LLC
TTT Record ID:	2024-8476

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EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Xaciato (clindamycin phosphate) vaginal gel 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 clindamycin vaginal gel, suppository, or cream products in pediatric patients.

Xaciato (clindamycin phosphate) vaginal gel is a lincosamide antibacterial first approved in the United States on December 7, 2021. It is currently indicated for the treatment of bacterial vaginosis in female patients 12 years of age and older. Clindamycin is available in vaginal gel, suppository, and cream formulations; FDA approved the first formulation for vaginal route of administration in 1992.

This pediatric postmarketing safety review was stimulated by pediatric labeling of Xaciato on initial approval on December 7, 2021, which included a pediatric indication.

A pediatric postmarketing pharmacovigilance review for clindamycin vaginal gel, suppository, or cream has not been previously presented before the Pediatric Advisory Committee.

DPV reviewed all serious FAERS reports with clindamycin vaginal gel, suppository, or cream in pediatric patients less than 17 years of age from August 11, 1992 – January 31, 2024 and identified two reports; 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 clindamycin vaginal gel, suppository, or cream in pediatric patients less than 17 years of age.

DPV did not identify any new pediatric safety concerns for clindamycin vaginal gel, suppository, or cream at this time. DPV will continue routine pharmacovigilance monitoring for clindamycin gel, suppository, or cream.

1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Xaciato (clindamycin phosphate) vaginal gel 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 clindamycin vaginal gel, suppository, or cream in pediatric patients.

1.1 PEDIATRIC REGULATORY HISTORY

Xaciato (clindamycin phosphate) vaginal gel is a lincosamide antibacterial first approved in the United States on December 7, 2021. It is currently indicated for the treatment of bacterial vaginosis in female patients 12 years of age and older.[1] Clindamycin is available in vaginal gel, suppository, or cream formulations.[a] FDA approved the first formulation for vaginal route of administration in 1992.

This pediatric postmarketing safety review was stimulated by pediatric labeling on initial approval of Xaciato on December 7, 2021, which included a pediatric indication.[2]

A pediatric postmarketing pharmacovigilance review for clindamycin vaginal gel, suppository, or cream has not been previously presented before the Pediatric Advisory Committee.

1.2 RELEVANT LABELED SAFETY INFORMATION

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

> ----------CONTRAINDICATIONS ----------
> History of hypersensitivity to clindamycin or lincomycin. (4.1)
>
> ----------WARNINGS AND PRECAUTIONS ----------
> - Clostridioides difficile-Associated Diarrhea: Discontinue and evaluate if diarrhea occurs. (5.1)
> - Use with Polyurethane Condoms: Polyurethane condoms are not recommended during treatment with XACIATO or for 7 days following treatment. During this time period, polyurethane condoms may not be reliable for preventing pregnancy or for protecting against transmission of HIV and other sexually transmitted diseases. Latex or polyisoprene condoms should be used (5.2)
>
> ----------ADVERSE REACTIONS ----------
> The most common adverse reactions reported in >2% of patients and at a higher rate in the XACIATO group than in the placebo group were vulvovaginal candidiasis and vulvovaginal discomfort. (6.1)
>
> **8.4 Pediatric Use**
>
> The safety and effectiveness of XACIATO have been established in females aged 12 years and older for the treatment of bacterial vaginosis. Use of XACIATO for this indication is supported by the extrapolation of clinical trial data from adequate and well controlled clinical studies in adult women. The safety and effectiveness of XACIATO have not been established in pediatric patients younger than 12 years of age for the treatment of bacterial vaginosis.

[a] Products include Xaciato (clindamycin phosphate) vaginal gel (NDA 215650), Cleocin (clindamycin phosphate) vaginal suppositories (NDA 050680, 050767), Clindesse (clindamycin phosphate) vaginal cream (NDA 050793), and as a generic clindamycin phosphate vaginal cream formulation (ANDA 065139).

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	February 22, 2024
Time period of search	August 11, 1992† - January 31, 2024
Search type	RxLogix Pediatric Focused Review Alert – DPV
Product terms	Product active ingredient: Clindamycin, clindamycin hydrochloride, clindamycin hydrochloride monohydrate, clindamycin phosphate
Other search terms	Dose route of administration: vaginal
MedDRA search terms (Version 26.1)	All Preferred Terms
* See Appendix A for a description of the FAERS database. † Date of approval for first clindamycin gel, suppository, or cream (NDA 050680) 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 August 11, 1992 – January 31, 2024, with clindamycin vaginal gel, suppository, or cream.

Table 2. Total Adult and Pediatric FAERS Reports* Received by FDA From August 11, 1992 – January 31, 2024, With Use of Clindamycin Vaginal Gel, Suppository, or Cream

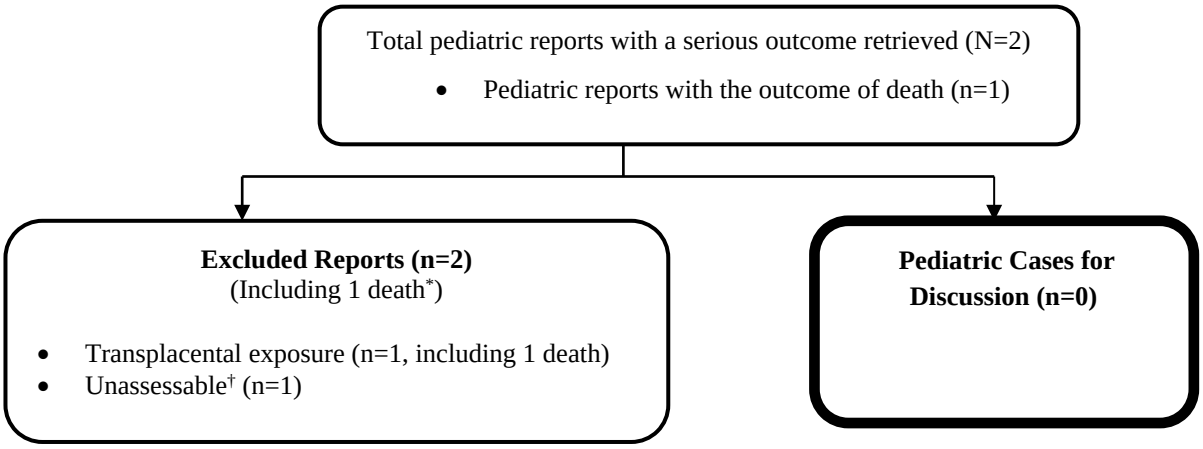
	All Reports (U.S.)	**Serious† (U.S.)**	**Death (U.S.)**
Adults (≥ 17 years)	247 (203)	140 (98)	4 (1)
Pediatrics (0 - < 17 years)	2‡ (2)	2‡ (2)	1‡ (1)

* 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.
‡ One additional report of U.S. pediatric deaths was identified among reports not reporting an age. This report is reflected in the counts of pediatric reports.

3.1.2 Selection of Serious Pediatric Cases in FAERS

Our FAERS search retrieved two serious pediatric reports from August 11, 1992 – January 31, 2024. We reviewed all FAERS pediatric reports with a serious outcome and excluded both reports 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 Clindamycin Vaginal Gel, Suppository, or Cream



* One excluded FAERS report described a fatal outcome. The death was determined to be not attributable to clindamycin.
† 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 clindamycin vaginal gel, suppository, or cream in pediatric patients less than 17 years of age from August 11, 1992 – January 31, 2024 and identified two reports; 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 clindamycin vaginal gel, suppository, or cream in pediatric patients less than 17 years of age.

5 CONCLUSION

DPV did not identify any new pediatric safety concerns for clindamycin vaginal gel, suppository, or cream at this time. DPV will continue routine pharmacovigilance monitoring for clindamycin vaginal gel, suppository, or cream.

6 REFERENCES

1. Xaciato (clindamycin phosphate) vaginal gel. [Prescribing information]. San Diego, CA; Dare Bioscience, Inc.: March 2023.
2. Xaciato (clindamycin phosphate) vaginal gel. [Prescribing information]. San Diego, CA; Dare Bioscience, Inc.: December, 2021.

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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