Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Pediatric Postmarketing Pharmacovigilance Review

Date:	June 18, 2020
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Product Name:	Xepi (ozenoxacin)
Pediatric Labeling Approval Date:	December 11, 2017
Application Type/Number:	NDA 208945
Applicant:	Ferrer Internacional S.A.
OSE RCM #:	2020-140

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EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Xepi (ozenoxacin) in pediatric patients through 17 years. The Division of Pharmacovigilance (DPV) conducted this review in accordance with the Food and Drug Administration Amendments Act (FDAAA) Pediatric Research Equity Act (PREA). This review focuses on serious unlabeled adverse events associated with ozenoxacin in pediatric patients.

The FDA approved ozenoxacin on December 11, 2017 and it is indicated for the treatment of impetigo. The approved pediatric labeling is for the treatment of impetigo in adolescents and children 2 months of age and older. However, commercial launch of this product in the United States did not occur until October 31, 2018.

The FAERS search retrieved a total of three reports for all patients. None of the three reports documented an age, and narrative details suggest the patients were adults. Only one case was serious and described a hypersensitivity reaction that responded to self-treatment with diphenhydramine.

DPV did not identify any new pediatric safety concerns for ozenoxacin at this time. DPV recommends no regulatory action at this time and will continue to monitor all adverse events associated with the use of ozenoxacin.

1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Xepi (ozenoxacin) in pediatric patients through 17 years. The Division of Pharmacovigilance (DPV) conducted this review in accordance with the Food and Drug Administration Amendments Act (FDAAA) Pediatric Research Equity Act (PREA). This review focuses on serious unlabeled adverse events associated with ozenoxacin in pediatric patients.

1.1 PEDIATRIC REGULATORY HISTORY

Ozenoxacin 1% cream is a non-fluorinated quinolone antibacterial that was approved on December 11, 2017 and is indicated for the topical treatment of impetigo due to *Staphylococcus aureus* or *Streptococcus pyogenes* in adult and pediatric patients 2 months of age and older. The medication was indicated for use in children at the time of approval. Commercial launch of this product in the United States did not occur until October 31, 2018.

Two trials were conducted with ozenoxacin 1% cream for the treatment of impetigo, and both trials included pediatric patients. Study P-110880-01 was a phase III, three-arm trial comparing ozenoxacin, placebo, and retapamulin 1% ointment (ClinicalTrials.gov Identifier: NCT01397461). A total of 465 patients two years of age and older were randomized to receive treatment twice daily for 5 days. Clinical response of ozenoxacin was found to be significantly superior compared to placebo, and no serious adverse events were reported in any of the three arms.

Study P-110881-01 was a phase III, two-arm, double-blind study to assess the efficacy and safety of ozenoxacin 1% cream versus placebo in the treatment of patients with impetigo (ClinicalTrials.gov Identifier: NCT02090764). A total of 412 patients aged two months and older were randomized to receive either ozenoxacin 1% cream or placebo for 5 days. Ozenoxacin was found to be significantly superior compared to placebo, and no serious adverse events were reported in either arm.

DPV has not previously presented ozenoxacin 1% cream before the Pediatric Advisory Committee.

1.2 RELEVANT LABELED SAFETY INFORMATION

The ozenoxacin labeling includes the following information under Highlights:

----------CONTRAINDICATIONS----------

- None

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

- Potential for Microbial Overgrowth: Prolonged use of XEPI may result in overgrowth of nonsusceptible bacteria and fungi. If such infections occur, discontinue use and institute alternative therapy.

----------ADVERSE REACTIONS----------

- Adverse reactions (rosacea and seborrheic dermatitis) were reported in 1 adult patient treated with XEPI.

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	January 22, 2020
Time period of search	December 11, 2017† - January 21, 2020
Search type	Quick Query
Product terms	Product active ingredient: Ozenoxacin Product name: Xepi
MedDRA Search Terms	All Preferred Terms (PT)
MedDRA version	22.1
* See Appendix B for a description of the FAERS database. † U.S. approval date	

3 RESULTS

3.1 FAERS

The FAERS search retrieved a total of three reports for all patients. None of the three reports documented an age, and narrative details suggest the patients were adults. Only one case was serious and described a hypersensitivity reaction that responded to self-treatment with diphenhydramine.

4 DISCUSSION

DPV reviewed all FAERS reports with ozenoxacin use from December 11, 2017 to January 21, 2020 and found no pediatric cases. Therefore, there were no new safety signals identified.

5 CONCLUSION

DPV did not identify any pediatric safety concerns for ozenoxacin at this time.

6 RECOMMENDATION

DPV recommends no regulatory action at this time and will continue to monitor all adverse events associated with the use of ozenoxacin.

7 APPENDICES

7.1 APPENDIX A. FDA ADVERSE EVENT REPORTING SYSTEM (FAERS)

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 or not 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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