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:	November 8, 2023
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Product Name:	Xtoro (finafloxacin otic suspension)
Pediatric Labeling Approval Date:	December 17, 2014
Application Type/Number:	NDA 206307
Applicant:	Fonseca Biosciences, LLC.
TTT Record ID:	2023-6128

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EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Xtoro (finafloxacin otic suspension) in pediatric patients less than 17 years of age. The Division of Pharmacovigilance (DPV) conducted this review in accordance with the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA). This review focuses on serious unlabeled adverse events associated with finafloxacin in pediatric patients.

Xtoro (finafloxacin otic suspension) is a quinolone antimicrobial initially approved in the U.S. on December 17, 2014. Xtoro is indicated for the treatment of acute otitis external (AOE) caused by susceptible strains of *Pseudomonas aeruginosa* and *Staphylococcus aureus*.

Of note, the Applicant for Xtoro has not marketed the product in the United States or elsewhere to date.

This pediatric postmarketing safety review was prompted by the pediatric labeling on initial approval on December 17, 2014, that included use in pediatric patients aged 1 year and older. A pediatric safety review for finafloxacin has not previously been presented to the Pediatric Advisory Committee.

DPV searched FAERS for all serious reports with finafloxacin in pediatric patients less than 17 years of age from December 17, 2014 – August 28, 2023, and did not identify any reports.

There were no new safety signals identified, no increased severity or frequency of any labeled adverse events, and no deaths directly associated with finafloxacin in pediatric patients less than 17 years of age. DPV did not identify any new pediatric safety concerns for finafloxacin at this time.

1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Xtoro (finafloxacin otic suspension) in pediatric patients less than 17 years of age. The Division of Pharmacovigilance (DPV) conducted this review in accordance with the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA). This review focuses on serious unlabeled adverse events associated with finafloxacin in pediatric patients.

1.1 PEDIATRIC REGULATORY HISTORY

Xtoro (finafloxacin otic suspension) is a quinolone antimicrobial initially approved in the U.S. on December 17, 2014. Xtoro is indicated for the treatment of acute otitis externa (AOE) caused by susceptible strains of *Pseudomonas aeruginosa* and *Staphylococcus aureus*.[1]

Of note, the Xtoro Applicant has not marketed the product in the U.S. or elsewhere to date.[2]

This pediatric postmarketing safety review was prompted by the pediatric labeling on initial approval on December 17, 2014, that included use in pediatric patients aged 1 year and older. A pediatric safety review for finafloxacin has not previously been presented to the Pediatric Advisory Committee.

1.2 RELEVANT LABELED SAFETY INFORMATION

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

> ----------CONTRAINDICATIONS----------
> None. (4)
> ----------WARNINGS AND PRECAUTIONS----------
> Prolonged use of this product may lead to overgrowth of non-susceptible organisms. Discontinue use if this occurs. (5.1)
> Allergic reactions may occur in patients with a history of hypersensitivity to finafloxacin, to other quinolones, or to any of the components in this medication. Discontinue use if this occurs. (5.2)
> ----------ADVERSE REACTIONS----------
> The most common adverse reactions occurring in 1% of patients with XTORO were ear pruritus and nausea. (6)
>
> **8.4 Pediatric Use**
> The safety and efficacy of XTORO in infants below one year of age have not been established. The safety and efficacy of XTORO in treating acute otitis externa in pediatric patients one year or older have been demonstrated in adequate and well controlled clinical trials [see CLINICAL STUDIES 14].

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 29, 2023
Time period of search	December 17, 2014† - August 28, 2023
Search type	RxLogix Post-Market Cases
Product terms	Product Active Ingredient: finafloxacin
MedDRA search terms (Version 26.0)	All Preferred Terms
* See Appendix A for a description of the FAERS database. † Xtoro 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 December 17, 2014 – August 28, 2023, with finafloxacin.

Table 2. Total Adult and Pediatric FAERS Reports* Received by FDA From December 17, 2014 – August 28, 2023, With Finafloxacin

	All Reports (U.S.)	Serious† (U.S.)	Death (U.S.)
Adults (≥ 17 years)	0 (0)	0 (0)	0 (0)
Pediatrics (0 - < 17 years)	0 (0)	0 (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 zero serious pediatric reports from December 17, 2014 – August 28, 2023.

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 finafloxacin in pediatric patients less than 17 years of age from December 17, 2014 – August 28, 2023, and did not identify any reports.

There were no new safety signals identified, no increased severity or frequency of any labeled adverse events, and no deaths directly associated with finafloxacin in pediatric patients less than 17 years of age.

5 CONCLUSION

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

6 REFERENCES

1. Xtoro (finafloxacin otic suspension). [Prescribing information]. Fort Worth, TX; Novartis: December, 2014.

2. NDA 206307 Xtoro (finafloxacin otic suspension) 0.3% Annual Report. December 14, 2022.

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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