Department of Health and Human Services
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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:	August 28, 2025
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Product Name:	Isopto Atropine (atropine sulfate ophthalmic solution)
Pediatric Labeling Approval Date:	December 1, 2016
Application Type/Number:	NDA 208151
Applicant:	Alcon Laboratories, Inc.
TTT Record ID:	2025-14961

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EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Isopto Atropine (atropine sulfate ophthalmic solution) 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 United States (U.S.) serious unlabeled adverse events associated with Isopto Atropine Solution in pediatric patients.

Isopto Atropine Solution (atropine sulfate ophthalmic solution) is a muscarinic antagonist and was initially FDA approved on December 1, 2016. Isopto Atropine is currently indicated for:

- Mydriasis
- Cycloplegia
- Penalization of the healthy eye in the treatment of amblyopia

Due to the potential for systemic absorption of atropine sulfate ophthalmic solution, use in children under the age of 3 months is not recommended and use in children under 3 years of age should be limited to no more than one drop per eye per day. Safety and efficacy in children above the age of 3 months has been established in adequate and well controlled trials.

This pediatric postmarketing safety review was prompted by pediatric labeling on December 1, 2016, that approved the use of Isopto Atropine in pediatric patients.

DPV reviewed all U.S. serious FAERS reports with Isopto Atropine in pediatric patients less than 17 years of age from December 1, 2016, through June 2, 2025, and identified two reports; however, both 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 Isopto Atropine in pediatric patients less than 17 years of age.

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

1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Isopto Atropine (atropine sulfate ophthalmic solution) 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 United States (U.S.) serious unlabeled adverse events associated with Isopto Atropine in pediatric patients.

1.1 PEDIATRIC REGULATORY HISTORY[1]

Isopto Atropine (atropine sulfate ophthalmic solution) is a muscarinic antagonist and was initially FDA approved on December 1, 2016. Isopto Atropine is currently indicated for:

- Mydriasis
- Cycloplegia
- Penalization of the healthy eye in the treatment of amblyopia

Due to the potential for systemic absorption of atropine sulfate ophthalmic solution, use in children under the age of 3 months is not recommended and use in children under 3 years of age should be limited to no more than one drop per eye per day. Safety and efficacy in children above the age of 3 months has been established in adequate and well controlled trials.

This pediatric postmarketing safety review was prompted by pediatric labeling on December 1, 2016 that approved the use of Isopto Atropine in pediatric patients.

A pediatric safety review for Isopto Atropine has not previously been presented to the Pediatric Advisory Committee.

1.2 RELEVANT LABELED SAFETY INFORMATION

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

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

- Hypersensitivity or allergic reaction to any ingredient in the formulation.

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

- Photophobia and blurred vision due to pupil unresponsiveness and cycloplegia may last up to 2 weeks.
- Risk of blood pressure increase from systemic absorption.
- Increased adverse drug reaction susceptibility with certain central nervous system conditions.

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

The most common adverse reactions that have been reported are eye pain and stinging on administration, blurred vision, photophobia, superficial keratitis, decreased lacrimation, drowsiness, increased heart rate and blood pressure.

----------USE IN SPECIFIC POPULATIONS----------

8.4 Pediatric Use

Due to the potential for systemic absorption of atropine sulfate ophthalmic solution the use of ISOPTO® Atropine 1% in children under the age of 3 months is not recommended and the use in children under 3 years of age should be limited to no more than one drop per eye per day. Safety and efficacy in children above the age of 3 months has been established in adequate and well controlled trials.

2 METHODS AND MATERIALS

DPV searched the FAERS database with the strategy described in Table 1.

Table 1. FAERS Search Strategy*

Date of search	June 3, 2025
Time period of search	December 1, 2016† - June 2, 2025
Search type	RxLogix Pediatric Focused Review Alert - DPV
Product terms	Product Name: Isopto atropine Case Application Number: NDA 208151
MedDRA search terms (Version 28.0)	All Preferred Terms

* See Appendix A for a description of the FAERS database.
† U.S. approval date for Isopto Atropine.
Abbreviation: MedDRA=Medical Dictionary for Regulatory Activities

3 RESULTS

3.1 SELECTION OF U.S. SERIOUS PEDIATRIC CASES IN FAERS

Our FAERS search retrieved two U.S. serious[a] pediatric reports for patients less than 17 years old from December 1, 2016, through June 2, 2025, including one report with the outcome of death. We excluded both reports from the case series for the reasons described below:

- Labeled adverse event not representing increased severity (n=1)
- Adverse event more likely due to concomitant medications or comorbidities (n=1, including 1 death)

One excluded U.S. FAERS report described a fatal outcome due to myeloid sarcoma disease progression. Death was not determined to be attributed to Isopto Atropine.

3.2 SUMMARY OF U.S. FATAL PEDIATRIC CASES (N=0)

There are no fatal pediatric adverse event cases for discussion.

[a] 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.

3.3 SUMMARY OF U.S. SERIOUS NON-FATAL PEDIATRIC CASES (N=0)

There are no non-fatal pediatric adverse event cases for discussion.

4 DISCUSSION

DPV reviewed all U.S. serious FAERS reports with Isopto Atropine in pediatric patients less than 17 years of age from December 1, 2016, through June 2, 2025, and identified two 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 Isopto Atropine in pediatric patients less than 17 years of age.

5 CONCLUSION

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

6 REFERENCES

1. Isopto Atropine (atropine sulfate ophthalmic solution). [package insert]. Fort Worth, TX. Alcon Laboratories, Inc. Revised August 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.