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:	March 24, 2025
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Product Name:	Ryaltris (olopatadine hydrochloride and mometasone furoate monohydrate nasal spray)
Pediatric Labeling Approval Date:	January 13, 2022
Application Type/Number:	NDA 211746
Applicant:	Glenmark Specialty SA
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EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Ryaltris (olopatadine hydrochloride and mometasone furoate monohydrate nasal spray) 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 olopatadine hydrochloride and mometasone furoate monohydrate in pediatric patients.

Ryaltris (olopatadine hydrochloride and mometasone furoate monohydrate nasal spray) is a combination of a histamine-1-receptor inhibitor and a corticosteroid, that was initially approved in the U.S. on January 13, 2022. Ryaltris is currently indicated for the treatment of symptoms of seasonal allergic rhinitis in adult and pediatric patients 12 years of age and older.

This pediatric postmarketing safety review was prompted by pediatric labeling at the time of initial approval on January 13, 2022, that included an indication for use in pediatric patients aged 12 years and older.

DPV has not previously performed a pediatric postmarketing pharmacovigilance review for olopatadine hydrochloride and mometasone furoate monohydrate for the Pediatric Advisory Committee.

DPV searched FAERS for all U.S. serious reports with olopatadine hydrochloride and mometasone furoate monohydrate in pediatric patients less than 17 years of age from January 13, 2022 – February 9, 2025, and did not identify any reports.

There were no new safety signals identified, no increased severity of any labeled adverse events, and no deaths directly associated with olopatadine hydrochloride and mometasone furoate monohydrate in pediatric patients less than 17 years of age.

DPV did not identify any new pediatric safety concerns for olopatadine hydrochloride and mometasone furoate monohydrate at this time and will continue routine pharmacovigilance monitoring for olopatadine hydrochloride and mometasone furoate monohydrate.

1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Ryaltris (olopatadine hydrochloride and mometasone furoate monohydrate nasal spray) 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 olopatadine hydrochloride and mometasone furoate monohydrate in pediatric patients.

1.1 PEDIATRIC REGULATORY HISTORY

Ryaltris (olopatadine hydrochloride and mometasone furoate monohydrate nasal spray) is a combination of a histamine-1-receptor inhibitor and a corticosteroid, that was initially approved in the U.S. on January 13, 2022.[1] Ryaltris is currently indicated for the treatment of symptoms of seasonal allergic rhinitis in adult and pediatric patients 12 years of age and older.[2]

This pediatric postmarketing safety review was prompted by pediatric labeling at the time of initial approval on January 13, 2022, that included an indication for use in pediatric patients aged 12 years and older.

DPV has not previously performed a pediatric postmarketing pharmacovigilance review for olopatadine hydrochloride and mometasone furoate monohydrate for the Pediatric Advisory Committee.

1.2 RELEVANT LABELED SAFETY INFORMATION

The Ryaltris (olopatadine hydrochloride and mometasone furoate monohydrate nasal spray) labeling contains the following safety information excerpted from the Highlights of Prescribing Information and the *Pediatric Use* subsection. For additional Ryaltris labeling information, please refer to the full prescribing information.[2]

----------CONTRAINDICATIONS----------
Patients with known hypersensitivity to any ingredients of RYALTRIS, including mometasone furoate. (4)

----------WARNINGS AND PRECAUTIONS----------
- Epistaxis, nasal ulcerations, nasal septal perforations, impaired wound healing, and Candida albicans infection: Monitor patients periodically for signs of adverse reactions on the nasal mucosa. (5.1)
- Somnolence: Avoid engaging in hazardous occupations requiring complete mental alertness and motor coordination such as driving or operating machinery when taking RYALTRIS. (5.2)
- Avoid concurrent use of alcohol or other central nervous system (CNS) depressants with RYALTRIS because additional reductions in alertness and additional impairment of CNS performance may occur. (5.2)
- Glaucoma and cataracts: Monitor patients with a change in vision or with a history of increased intraocular pressure, glaucoma, and/or cataracts. (5.3)
- Hypersensitivity Reactions: Hypersensitivity reactions can occur with RYALTRIS. Hypersensitivity reactions including wheezing, have occurred after the nasal administration of mometasone furoate. Discontinue RYALTRIS if such reactions occur. (5.4)
- Immunosuppression and Risk of Infections: Potential worsening of existing tuberculosis; fungal, bacterial, viral, or parasitic infections; or ocular herpes simplex. More serious or even fatal course of chickenpox or measles in susceptible patients: Use caution in patients with the above because of the potential for worsening of these infections. (5.5)
- Hypercorticism and adrenal suppression with misuse or use of higher than-recommended dosages or at the regular dosage in susceptible patients at risk for such effects (5.6)

- Potential reduction in growth velocity in children: Routinely monitor the growth in pediatric patients receiving RYALTRIS. (5.7, 8.4)

----------ADVERSE REACTIONS----------
The most common adverse reactions (≥1% incidence) are dysgeusia, epistaxis, and nasal discomfort. (6.1)

8.4 Pediatric Use

The safety and effectiveness of RYALTRIS for the treatment of symptoms associated with seasonal allergic rhinitis have been established in pediatric patients 12 years and older. Use of RYALTRIS for this indication is supported by evidence from adequate and well-controlled studies in adult and pediatric patients 12 years and older [see Clinical Studies (14)].

The safety and effectiveness of RYALTRIS in pediatric patients below the age of 12 years have not been established.

Effect on Growth
Controlled clinical studies have shown that nasal corticosteroids may cause a reduction in growth velocity in pediatric patients. This effect has been observed in the absence of laboratory evidence of HPA axis suppression, suggesting that growth velocity is a more sensitive indicator of systemic corticosteroid exposure in pediatric patients than some commonly used tests of HPA axis function. The long-term effects of this reduction in growth velocity associated with nasal corticosteroids, including the impact on final adult height, are unknown. The potential for "catch up" growth following discontinuation of treatment with nasal corticosteroids has not been adequately studied.

The growth of pediatric patients receiving nasal corticosteroids, including RYALTRIS, should be monitored routinely (e.g., via stadiometry). The potential growth effects of prolonged treatment should be weighed against clinical benefits obtained and the risk/benefits of non-corticosteroid treatment alternatives.

The potential of mometasone furoate nasal spray 50 mcg to cause growth suppression in susceptible patients or when given at higher doses cannot be ruled out.

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 10, 2025
Time period of search	January 13, 2022† - February 9, 2025
Search type	RxLogix Pediatric Focused Review Alert – DPV
Product terms	Product active ingredient: Mometasone furoate monohydrate\Olopatadine hydrochloride
MedDRA search terms (Version 27.1)	All Preferred Terms
Other search terms‡	Case Seriousness: Serious Country Derived: USA
* See Appendix A for a description of the FAERS database. † Ryaltris U.S. approval date ‡ 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. Abbreviations: MedDRA=Medical Dictionary for Regulatory Activities; USA=United States of America	

3 RESULTS

3.1 FAERS

3.1.1 Selection of U.S. Serious Pediatric Cases in FAERS

Our FAERS search retrieved zero U.S. serious pediatric reports for patients less than 17 years old from January 13, 2022 – February 9, 2025.

3.1.2 Summary of U.S. Fatal Pediatric Cases (N=0)

There are no fatal pediatric adverse event cases for discussion.

3.1.3 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 searched FAERS for all U.S. serious reports with olopatadine hydrochloride and mometasone furoate monohydrate in pediatric patients less than 17 years of age from January 13, 2022 – February 9, 2025, and did not identify any reports.

There were no new safety signals identified, no increased severity of any labeled adverse events, and no deaths directly associated with olopatadine hydrochloride and mometasone furoate monohydrate in pediatric patients less than 17 years of age.

5 CONCLUSION

DPV did not identify any new pediatric safety concerns for olopatadine hydrochloride and mometasone furoate monohydrate at this time and will continue routine pharmacovigilance monitoring for olopatadine hydrochloride and mometasone furoate monohydrate.

6 REFERENCES

1. Ryaltris (olopatadine hydrochloride and mometasone furoate monohydrate nasal spray). [Prescribing information]. Columbus, OH; Glenmark Specialty SA: January 2022.
2. Ryaltris (olopatadine hydrochloride and mometasone furoate monohydrate nasal spray). [Prescribing information]. Columbus, OH; Glenmark Specialty SA: August 2023.

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.