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

Date:	April 27, 2020
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Product Name:	Lumify (brimonidine tartrate) OTC
Pediatric Labeling Approval Date:	December 22, 2017
Application Type/Number:	NDA 208144
Applicant:	Bausch and Lomb INC
OSE RCM #:	2020-241

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EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports associated with Lumify 0.025% (brimonidine tartrate) ophthalmic solution in pediatric patients through age 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 Lumify in pediatric patients from December 22, 2016 (one year prior to approval date of pediatric labeling) through February 2, 2020.

FDA approved Lumify on December 22, 2017 and it is indicated for over-the-counter use for the relief of redness of the eye due to minor eye irritations in adults and children 5 years of age and over.

DPV retrieved one pediatric FAERS case from December 22, 2016 through February 2, 2020. We excluded this case because it was nonserious and the adverse event of *Eye redness* was confounded by the product indication 'relief of redness of the eye.' We did not identify any relevant serious non-fatal or fatal pediatric cases associated with Lumify to include in a case series.

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

1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports associated with Lumify 0.025% (brimonidine tartrate) ophthalmic solution in pediatric patients through age 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 Lumify in pediatric patients from December 22, 2016 (one year prior to approval date of pediatric labeling) through February 2, 2020.

1.1 PEDIATRIC REGULATORY HISTORY

FDA approved Lumify 0.025% ophthalmic solution on December 22, 2017 for over-the-counter (OTC) use for the relief of redness of the eye due to minor eye irritations in adults and children 5 years of age and over.[1] The pediatric study requirement for ages 5 to 17 years was fulfilled with this application.[1] DPV has not previously reviewed Lumify for the Pediatric Advisory Committee (PAC).

1.2 SUMMARY OF DIVISION OF NONPRESCRIPTION DRUG PRODUCTS CLINICAL REVIEW

The Division of Nonprescription Drug Products (DNDP) reviewed the safety profile of Lumify in the Clinical Review dated October 31, 2017. DNDP found that the provided safety data supported the safe use of brimonidine tartrate in the intended pediatric age population of 5 to less than 17 years of age and therefore fulfilled its PREA requirement.[2]

Pediatric subjects (age 5 to 17 years) comprised 7.9% (50/638) of the study population from the brimonidine tartrate 0.025% clinical trials.[2] Somnolence was assessed in safety study CSR 13-100-0006 because of the higher incidence of systemic adverse effects such as somnolence and fatigue in children with more severe and frequent symptoms at a younger age following exposure to brimonidine tartrate.[3] No evidence of somnolence or change in alertness was observed in children aged 5 to 17 years.[2]

DNDP concluded that "a*lthough this product may provide relief of the symptoms from such conditions safely when used as intended, there are other OTC eye drops available that may be a more appropriate choice to treat allergic conjunctivitis. However, the proposed labeling directs consumers to stop use and ask a doctor if conditions worsens or persists for more than 72 hours. This labeling reduces the risk of significant delay of treatment of underlying ocular disease."*[2]

FDA waived the *"pediatric study requirement for ages 0 to 4 years because the product does not represent a meaningful therapeutic benefit over therapies for pediatric patients in this age group and is not likely to be used in a substantial number of pediatric patients in this group."*[1,a]

1.3 RELEVANT LABELED SAFETY INFORMATION

The following warnings are included on the OTC drug facts label for Lumify[4]:

- For external use only
- Do not use if solution changes color or becomes cloudy
- Stop use and ask a doctor
    - If you experience eye pain, changes in vision, continued redness or irritation of the eye
    - Condition worsens or persists for more than 3 days
- If pregnant or breast-feeding, ask a health professional before use.
- Keep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right away.

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 3, 2020
Time period of search	December 22, 2016† - February 2, 2020
Search type	FBIS Quick Query
Product terms	Product name: Lumify Product NDA#: 208144
MedDRA search terms (Version 22.1)	All preferred terms
Age (years)	0-17
* See **Appendix A** for a description of the FAERS database. † One year prior to approval date of pediatric labeling.	

3 RESULTS

3.1 FAERS

3.1.1 Total Number of FAERS Reports by Age

[a] According to the clinical review by DNDP, *"a partial waiver of studies in pediatric patients 0 to 4 years of age was granted on the basis that evidence strongly suggests this drug would be unsafe in this age group. The proposed labeling does not include dosing instructions for children less than 5 years of age. The Division also agreed to the extrapolation of the efficacy of brimonidine tartrate 0.025% for reducing eye redness down to 5 years of age provided that safety was demonstrated."*[2]

Table 2 presents the number of adult and pediatric FAERS reports from December 22, 2016 through February 2, 2020 with Lumify.

Table 2. Total Adult and Pediatric FAERS Reports* Received by FDA From December 22, 2016 through February 2, 2020 With Lumify

	All reports (U.S.)	Serious† (U.S.)	Death (U.S.)
Adults (> 17 years)	421 (404)	37 (20)	1 (0)
Pediatrics (0 - 17 years)	1 (1)	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 Pediatric Cases in FAERS

DPV retrieved one pediatric FAERS case from December 22, 2016 through February 2, 2020. We excluded this case because it was nonserious and the adverse event of *Eye redness* was confounded by the product indication 'relief of redness of the eye'. We did not identify any relevant serious, non-fatal or fatal pediatric cases associated with Lumify to include in a case series.

4 DISCUSSION

We did not identify any serious non-fatal or fatal pediatric cases with Lumify.

5 CONCLUSION

DPV did not identify any unexpected safety concerns in the pediatric population for Lumify.

6 RECOMMENDATION

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

7 REFERENCES

1. Mahoney KM. NDA 208144, NDA approval letter. December 22, 2017. Accessed on February 10, 2020 at https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2017/208144Orig1s000ltr.pdf.
2. Kelty JL. NDA 208144, clinical review brimonidine tartrate ophthalmic solution, 0.025%. October 31, 2017. DARRTS Reference ID: 4174643.
3. Nevitt MP. NDA 208144, clinical review brimonidine tartrate ophthalmic solution, 0.025%. October 31, 2017. DARRTS Reference ID: 4175781.
4. Lumify (brimonidine tartrate ophthalmic solution 0.025%) [Drug facts label]. Bausch and Lomb. Bridgewater, NJ. April 2019.

8 APPENDICES

8.1 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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