**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

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| **Date:** | November 9, 2023 |
| **Reviewers:** | Debra Ryan, PharmD, MBA, Safety Evaluator<br>Ivone Kim, MD, Medical Officer<br>Division of Pharmacovigilance I (DPV-I) |
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| **Product Name:** | Baqsimi (glucagon) nasal powder |
| **Pediatric Labeling Approval Date:** | July 24, 2019 |
| **Application Type/Number:** | NDA 210134 |
| **Applicant:** | Eli Lilly and Company |
| **TTT Record ID:** | 2023-5966 |

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## EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Baqsimi (glucagon) nasal powder 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 U.S. serious unlabeled adverse events associated with Baqsimi in pediatric patients.

Baqsimi (glucagon) nasal powder is an antihypoglycemic agent approved in the U.S. on July 24, 2019. Baqsimi is currently indicated for the treatment of severe hypoglycemia in adult and pediatric patients with diabetes ages 4 years and above.

This pediatric postmarketing safety review was stimulated by pediatric labeling upon Baqsimi approval on July 24, 2019, that included use in pediatric patients with diabetes ages 4 years and above.

DPV reviewed two U.S. serious FAERS reports with Baqsimi in the pediatric population (ages 0 - <17 years) from July 24, 2019, through August 10, 2023. The two reports did not provide sufficient clinical detail to assess causality. We identified no new safety signals, no increased severity or frequency of any labeled adverse events, and no pediatric deaths associated with Baqsimi.

DPV did not identify any new pediatric safety concerns for Baqsimi at this time and will continue to monitor all adverse events associated with the use of Baqsimi.

# 1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Baqsimi (glucagon) nasal powder 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 U.S. serious unlabeled adverse events associated with Baqsimi in pediatric patients.

## 1.1 PEDIATRIC REGULATORY HISTORY[1]

Baqsimi (glucagon) nasal powder is an antihypoglycemic agent approved in the U.S. on July 24, 2019. Baqsimi is currently indicated for the treatment of severe hypoglycemia in adult and pediatric patients with diabetes ages 4 years and above.

This pediatric postmarketing safety review was stimulated by pediatric labeling upon Baqsimi approval on July 24, 2019, that included use in pediatric patients with diabetes ages 4 years and above.

DPV has not previously presented an evaluation of postmarketing adverse event reports for Baqsimi in pediatric patients to the Pediatric Advisory Committee.

## 1.2 RELEVANT LABELED SAFETY INFORMATION[2]

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

**----------CONTRAINDICATIONS----------**

- Pheochromocytoma
- Insulinoma
- Known hypersensitivity to glucagon or to any of the excipients

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

- Substantial Increase in Blood Pressure in Patients Pheochromocytoma: Contraindicated in patients with pheochromocytoma because BAQSIMI may stimulate the release of catecholamines from the tumor.
- Hypoglycemia in Patients with Insulinoma: In patients with insulinoma, administration may produce an initial increase in blood glucose; however, BAQSIMI may stimulate exaggerated insulin release from an insulinoma and cause hypoglycemia. If a patient develops symptoms of hypoglycemia after a dose of BAQSIMI, give glucose orally or intravenously.
- Hypersensitivity and Allergic Reactions: Allergic reactions have been reported and include generalized rash, and in some cases anaphylactic shock with breathing difficulties, and hypotension.

- Lack of Efficacy in Patients with Decreased Hepatic Glycogen: BAQSIMI is effective in treating hypoglycemia only if sufficient hepatic glycogen is present. Patients in states of starvation, with adrenal insufficiency or chronic hypoglycemia may not have adequate levels of hepatic glycogen for BAQSIMI to be effective. Patients with these conditions should be treated with glucose.

**----------ADVERSE REACTIONS----------**

- Most common (≥10%) adverse reactions associated with BAQSIMI are nausea, vomiting, headache, upper respiratory tract irritation (i.e., rhinorrhea, nasal discomfort, nasal congestion, cough, and epistaxis), watery eyes, redness of eyes, itchy nose, throat and eyes.

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

**8.4 Pediatric Use**

The safety and effectiveness of BAQSIMI for the treatment of severe hypoglycemia in patients with diabetes have been established in pediatric patients ages 4 years and above. Use of BAQSIMI for this indication is supported by evidence from a study in 48 pediatric patients from 4 to <17 years of age with type 1 diabetes mellitus.

The safety and effectiveness of BAQSIMI have not been established in pediatric patients younger than 4 years of age.

**----------CLINICAL STUDIES----------**

**14.2 Pediatric Patients**

Study 3 (NCT01997411) was a randomized, multicenter, clinical study that assessed BAQSIMI compared to intramuscular glucagon (IMG) in pediatric patients aged 4 years and older with type 1 diabetes. Insulin was used to reduce blood glucose levels, and glucagon was administered after glucose reached <80mg/dL. Efficacy was assessed based on percentage of patients with a glucose increase of ≥20 mg/dL L from glucose nadir within 30 minutes following BAQSIMI administration.

Forty-eight patients were enrolled and received at least one dose of study drug. The mean age in the Young Children cohort (4 to <8 years) was 6.5 years. In the Children cohort (8 to <12 years), mean age was 11.1 years and in the Adolescents cohort (12 to <17 years) mean age was 14.6 years. In all age cohorts, the population was predominantly male and white.

Across all age groups, all (100%) patients in both treatment arms achieved an increase in glucose ≥20 mg/dL from glucose nadir within 20 minutes of glucagon administration.

# 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 11, 2023 |
| Time period of search | July 24, 2019† - August 10, 2023 |
| Search type | RxLogix Post-Market Cases Quick Query |
| Product terms | Product Name: Baqsimi |
| MedDRA search terms (Version 26.0) | All Preferred Terms |
| *See Appendix A for a description of the FAERS database.<br>† U.S. approval date for Baqsimi.<br>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 July 24, 2019 through August 10, 2023, with Baqsimi.

| **Table 2. Total Adult and Pediatric FAERS Reports* Received by FDA From July 24, 2019 – August 10, 2023 for Baqsimi** | | | |
|---|---|---|---|
| | **All Reports (U.S.)** | **Serious† (U.S.)** | **Death (U.S.)** |
| Adults (≥ 17 years) | 112 (89) | 47 (24) | 2 (2) |
| Pediatrics (0 - < 17 years) | 15 (9) | 8 (2) | 0 (0) |
| * May include duplicates and transplacental exposures, and have not been assessed for causality<br>† 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 U.S. Serious Pediatric Cases in FAERS*

The FAERS search retrieved two U.S. serious pediatric reports from July 24 2019, through August 10, 2023. DPV reviewed these reports and excluded them from further discussion as they do not provide sufficient clinical detail to assess causality.

### *3.1.3 Summary of U.S. Fatal Pediatric Cases (N=0)*

We did not identify any FAERS U.S. fatal adverse event cases associated with Baqsimi in the pediatric population.

### *3.1.4 Summary of U.S. Serious Non-Fatal Pediatric Cases (N=0)*

We did not identify any FAERS U.S. serious, unlabeled, non-fatal adverse event cases associated with Baqsimi in the pediatric population for further discussion.

## 4 DISCUSSION

DPV reviewed two U.S. serious FAERS reports with Baqsimi in the pediatric population (ages 0 - <17 years) from July 24, 2019, through August 10, 2023. The two reports did not provide sufficient clinical detail to assess causality. We identified no new safety signals, no increased severity or frequency of any labeled adverse events, and no pediatric deaths associated with Baqsimi.

## 5 CONCLUSION

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

## 6 REFERENCES

1. Drug Approval Package: Baqsimi. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2019/210134Orig1s000TOC.cfm Accessed: August 14, 2023

2. Baqsimi (glucagon nasal powder) [package insert]. Indianapolis, IN. Eli Lilly and Company. Revised October 2020.

# 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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