BAQSIMI (glucagon) nasal powder Medical Value Summary

I. INDICATION[1]

- BAQSIMI™ is an antihypoglycemic agent indicated for the treatment of severe hypoglycemia in patients with diabetes ages 4 years and above.

II. DOSAGE AND ADMINISTRATION[1]

- Instruct patients and their caregivers on the signs and symptoms of severe hypoglycemia. Because severe hypoglycemia requires the help of others to recover, instruct the patient to inform those around them about BAQSIMI and its Instructions for Use. Administer BAQSIMI as soon as possible when severe hypoglycemia is recognized.
- Do not push the plunger or test the device prior to administration.
- Baqsimi is for intranasal use only.
- The recommended dose of BAQSIMI is 3 mg administered as one actuation of the intranasal device into one nostril.
- Administer Baqsimi according to the printed instructions on the shrink-wrapped tube label and the Instructions for Use.
- Administer the dose by inserting the tip into one nostril and pressing the device plunger all the way in until the green line is no longer showing. The dose does not need to be inhaled.
- Call for emergency assistance immediately after administering the dose.
- When the patient responds to treatment, give oral carbohydrates.
- Do not attempt to reuse Baqsimi. Each Baqsimi device contains one dose of glucagon and cannot be reused.
- If there has been no response after 15 minutes, an additional 3 mg dose may be administered while waiting for emergency assistance.

III. DOSAGE FORMS AND STRENGTHS[1]

- Nasal powder: intranasal device containing one dose of glucagon 3 mg

IV. EFFICACY SUMMARY[1,2]

- Baqsimi has been studied in patients with Type 1 Diabetes Mellitus (T1DM) in both adult and pediatric (≥4 years old) patient populations. Baqsimi has also been studied in a small subset of adult patients with Type 2 Diabetes Mellitus (T2DM).
- The studies below (Study 1 and Study 2) were non-inferiority studies comparing 3mg of Nasal Glucagon (NG) to 1 mg of intra-muscular glucagon (IMG) in adult patients.
- Treatment success was defined as patients achieving plasma glucose ≥70 mg/dL or increase of ≥20 mg/dL from glucose nadir within 30 minutes of administration.

	STUDY 1	STUDY 2
Patient Population	Adult patients with T1DM (N=66)	Adult patients (18 to <65 yo) with T1DM and T2DM (N=80)
Results	Non-inferior	Non-inferior
NG Treatment Success (%)	100	98.8[a,b]
IMG Treatment Success (%)	100	100
Mean time to treatment success (NG vs IMG)	NG: 11.6 min IMG: 9.9 min	NG: 15.9 min IMG: 12.1 min

a: One patient with T1DM reached treatment success after 40 min without additional intervention
b: 100% of 5 patients with T2DM included in the efficacy analysis met treatment success with BAQSIMI and injectable glucagon.

- The pediatric study looked at the proportion of participants who achieved an increase in glucose of ≥20 mg/dL from nadir within 30 min after receiving study glucagon.
  - Participants in the 4 to <8 years old and 8 to <12 years old cohorts were randomly allocated in a 2:1 ratio to receive either NG 2 mg and 3 mg (at Visit 1 and Visit 2 in a crossover manner) or weight-based IMG (0.5 mg or 1 mg at Visit 1 only, dependent on body weight in accordance with the approved recommended dose). The study was designed to compare the two NG doses with each other and with weight-based IMG.
  - Participants in the 12 <17 years old cohort were randomly allocated in a 1:1 ratio to receive either NG 3mg or IMG 1mg in Visit 1 and then the other glucagon preparation in Visit 2 in a crossover design.

	Cohort 1		Cohort 2		Cohort 3	
Patient Population	4 to <8 years old		8 to <12 years old		12 to <17 years old	
	Baqsimi 3mg	**IMG**	**Baqsimi 3mg**	**IMG**	**Baqsimi 3mg**	**IMG**
Treatment Success (%)	100	100	100	100	100	100
Mean time to ≥20 mg/dL from nadir (min)	10.8	10.8	11.3	12.5	14.2	12.5

- A clinical study evaluated nasal congestion and/or discharge from a common cold (with or without nasal decongestant use) in adult participants aged 18 to 50 years old.[3]
  - There were no clinically relevant differences in the glucagon PK and PD profiles after Baqsimi treatment in participants with a common cold (with or without nasal decongestant use) and participants with no cold symptoms.
  - Glucose and glucagon levels increased rapidly to peak glucose levels at 30 to 40 minutes post dose and to peak glucagon levels at 20 minutes post dose for all adult participants and were not significantly affected by nasal congestion and/or nasal discharge (with or without nasal decongestant use)
- In a simulated rescue study, Baqsimi had approximately a 90% administration success rate in both the trained and untrained arms versus 15.8% in the IMG trained arm and 0% in the IMG untrained arm. The median time to successful administration in the NG group was 30 seconds vs 73 seconds for IMG in trained users.[4]

V. SAFETY SUMMARY[1]

- **Please see full prescribing information available at:** http://pi.lilly.com/us/baqsimi-uspi.pdf
- BAQSIMI is contraindicated in patients with pheochromocytoma, insulinoma, and known hypersensitivity to glucagon or to any of the excipients in BAQSIMI.
- Contraindicated in patients with pheochromocytoma because BAQSIMI may stimulate the release of catecholamines from the tumor.
- Lack of Efficacy 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.
- 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 administration to be effective. Patients with these conditions should be treated with glucose.
- The most common pooled adverse reactions from adult studies 1 and 2 (incidence ≥2%) were nausea (26.1%), headache (18.3%), vomiting (15.0%) and upper respiratory tract irritation (12.4%; included rhinorrhea, nasal discomfort, nasal congestion, cough and epistaxis)
- Other observed adverse reactions with BAQSIMI-treated patients across clinical trials were, dysgeusia, pruritus, tachycardia, hypertension, and additional upper respiratory tract irritation events (nasal pruritus, throat irritation, and parosmia).

VI. REAL-WORLD EVIDENCE[5,6]

- An economic impact model of NG versus injectable glucagon (IG) for Commercial, Medicare Advantage and Managed Medicaid Plans projected lower mean total costs per severe hypoglycemic event.
    - NG and IG were separately assessed using the base model. This model is based on a treatment pathway covering decisions/outcomes following a severe hypoglycemic event and successful administration of full doses of rescue glucagon therapy by caregivers and acquaintances.
        - Probabilities and costs for treatment decisions and outcomes were sourced from NG Usability Studies, literature, expert judgement and IBM Marketscan.
        - The model assumed that 2019 Wholesale Acquisition Costs (WAC) for NG is equal to the WAC for IG. Reimbursement to pharmacy was estimated as Average Whole Price (AWP) minus 15% minus $25 copayment – with AWP being 20% greater than WAC. All costs were estimated in 2019 dollars. Costs estimates from earlier years were converted to 2019 dollars using the US Bureau of Labor and Statistics CPI-All Urban Consumers (Current Series).
        - The model estimated that the mean total costs per severe hypoglycemic event were lower for NG as compared to IG driven by lower EMS with transport and Emergency Department costs by: $929 for Commercial lives, $502 for Medicare Advantage lives, and $335 for Managed Medicaid lives.
- A study comparing the overall attitudes toward NG and autoinjector (AI) glucagon for the treatment of severe hypoglycemia among patients with T1DM and T2DM on insulin, caregivers of person with diabetes, and acquaintances of persons with diabetes was done in two phases. This study was done pre-approval of the AI device. It was completed with pre-regulatory approval perceptions of the AI device images and brief draft instructions.
    - Phase 1: Included one-on-one qualitative interviews via telephone with 15 patients with diabetes, 15 caregivers, and 15 acquaintances where participant perspectives of NG and AI were elicited. Participants were shown draft instructions of each device.
        - Results: 73% preferred NG over AI
    - Phase 2: Pilot study of Glucagon Device Preference Questionnaire (GDPQ) where 50 Participants (16 adults with diabetes on insulin, 18 caregivers, and 16 acquaintances) completed the questionnaire online and in One-on-one interviews to obtain feedback on GDPQ based on draft instructions for use.
        - GDPQ content:
            - 33 Rating items asked of each device (7- point rating scales, ranging from 'very unlikely' to 'very likely' or 'not at all' to 'extremely')
            - 16 Preference elicitation questions asking which device is preferred (7-point scale ranging from 'Very strongly prefer NG' to 'Very strongly prefer AI')
            - Conceptual framework developed grouping items into 3 scales: Ease of Use, Hesitancy with Device, and Feeling Prepared and Protected
        - Results: GDPQ differentiated attitudes between NG versus AI glucagon and more participants preferred NG to AI on all direct preference items. More participants favored nasal glucagon over autoinjector glucagon with respect to 'Ease of use', 'Feeling prepared and protected' and 'Hesitation in using device.'

VII. VALUE SUMMARY[1-6]

- Baqsimi has demonstrated non-inferiority to IMG as a rescue medication for severe hypoglycemic events in adult patients with T1DM and T2DM.
- Available as an intranasal device with no reconstitution necessary.
- In a simulated rescue study, Baqsimi had a 90% administration success rate in both the trained and untrained arms versus 15.8% in the IMG trained arm and 0% in the IMG untrained arm.
- Baqsimi has greater cost offsets per severe hypoglycemic event compared to injectable glucagon.
- A preliminary analysis done prior to autoinjector approval has shown that more patient with diabetes, caregivers, and acquaintances preferred Baqsimi to an autoinjector noting its ease of use.

REFERENCES

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4. Settles J, Child CJ, Bajpai S, et al. Nasal vs. Injected Glucagon: User Experience Results of a Simulated Severe Hypoglycemia Study. Poster presented at: American Diabetes Association's 79th Scientific Sessions; June 9, 2019; San Francisco, CA USA. Published online by Diabetes®. https://ada.apprisor.org/epsAbstractADA.cfm?id=1
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