



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

Amsterdam, 25 July 2024  
EMA/307732/2024

## Assessment report for paediatric studies submitted according to Article 46 of the Regulation (EC) No 1901/2006

### **BAQSIMI**

Glucagon

Procedure no: EMEA/H/C/003848/P46/002

### **Note**

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.



| Status of this report and steps taken for the assessment |                                           |              |             |                                  |
|----------------------------------------------------------|-------------------------------------------|--------------|-------------|----------------------------------|
| Current step <sup>1</sup>                                | Description                               | Planned date | Actual Date | Need for discussion <sup>2</sup> |
| <input type="checkbox"/>                                 | Start of procedure                        | 27/05/2024   | 27/05/2024  | <input type="checkbox"/>         |
| <input type="checkbox"/>                                 | CHMP Rapporteur Assessment Report         | 01/07/2024   | 27/06/2024  | <input type="checkbox"/>         |
| <input type="checkbox"/>                                 | CHMP members comments                     | 15/07/2024   | 15/07/2024  | <input type="checkbox"/>         |
| <input type="checkbox"/>                                 | Updated CHMP Rapporteur Assessment Report | 18/07/2024   | 18/07/2024  | <input type="checkbox"/>         |
| <input checked="" type="checkbox"/>                      | CHMP adoption of conclusions              | 25/07/2024   | 25/07/2024  | <input type="checkbox"/>         |

<sup>1</sup> Tick the box corresponding to the applicable step – do not delete any of the steps. If not applicable, add n/a instead of the date.

<sup>2</sup> Criteria for CHMP plenary discussion: substantial disagreement between the Rapporteur and other CHMP members and/or at the request of the Rapporteur or the Chair

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# 1. Introduction

On April 25, 2024, the MAH submitted a final study report for the completed paediatric study I8R-MC-IGBO for Basimi, in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

These data are also submitted as part of the post-authorisation measure.

A critical expert overview has also been provided.

# 2. Scientific discussion

## 2.1. Information on the development program

The MAH stated that Study I8R-MC-IGBO is part of a clinical development program. This is an Open-Label, Multi-Center, Single-Dose Study to Assess the Safety, Tolerability, Pharmacodynamics, and Pharmacokinetics of Nasal Glucagon in Paediatric Patients with Type 1 Diabetes Aged 1 to <4 years.

MAH also intends to submit the same data as part of a type II variation application in order to extend the indication of Baqsimi in the paediatric population (1 to <4 years) in Q4 2024.

## 2.2. Information on the pharmaceutical formulation used in the study

The same drug-device combination product that is already approved for use in adults, adolescents, and children aged 4 years and older was used in this study.

## 2.3. Clinical aspects

### 2.3.1. Introduction

The MAH submitted a final report for Study I8R-MC-IGBO.

**Study I8R-MC-IGBO** is an Open-Label, Multi-Center, Single-Dose Study to Assess the Safety, Tolerability, Pharmacodynamics, and Pharmacokinetics of Nasal Glucagon in Pediatric Patients with Type 1 Diabetes Aged 1 to <4 years.

## Description

## Methods

### Study participants

#### Disposition of Participants

7 participants enrolled in the study; all received the planned 3-mg dose of NG and completed the study.

#### Protocol Deviations

The protocol deviations that occurred were reviewed by the sponsor and were considered unlikely to have affected the safety of the participants or the results or conclusions presented in this report. There were no significant GCP issues.

Two deviations related to PK and PD collections were considered important, comprising

- a missing PK collection at the 60-minute post-dose time point for 1 participant
- a collection of the baseline PD sample 2 minutes outside of the predefined window for 1 participant.

### Demographic and Other Baseline Characteristics

Of the 7 participants enrolled in the study,

- all were white
- age ranged from 1.8 to 4 years old. It should be noted that the participant reported as 4 years old was actually less than 4 years old at screening and throughout the study, per protocol, but age was reported as 4 years due to the rounding of age in months for age derivation.
- body mass index ranged from 15.0 to 19.6 kg/m<sup>2</sup>
- duration of T1D ranged from 0.7 to 2.5 years.

**Table 1 Participant Demographics and Baseline Characteristics**

| Participant Demographics for Study I8R-MC-IGBO |                          |                     |
|------------------------------------------------|--------------------------|---------------------|
| Population: Safety                             |                          | 3 mg nasal glucagon |
| Number of participants studied                 |                          | 7                   |
| Age (years)                                    | Mean (SD)                | 2.98 (0.82)         |
|                                                | Range                    | 1.8 - 4.0           |
| Sex                                            | Male                     | 4 ( 57.1%)          |
|                                                | Female                   | 3 ( 42.9%)          |
| Ethnicity                                      | Not Hispanic or Latino   | 6 ( 85.7%)          |
|                                                | Hispanic or Latino       | 1 ( 14.3%)          |
| Race                                           | White                    | 7 (100.0%)          |
| Site ID                                        | 00001                    | 1 ( 14.3%)          |
|                                                | 00002                    | 1 ( 14.3%)          |
|                                                | 00004                    | 1 ( 14.3%)          |
|                                                | 00007                    | 2 ( 28.6%)          |
|                                                | 00008                    | 2 ( 28.6%)          |
| Country of Enrollment                          | United States of America | 7 (100.0%)          |
| Weight (kg)                                    | Mean (SD)                | 15.49 (2.36)        |
|                                                | Range                    | 12.2 - 18.6         |
| Height (cm)                                    | Mean (SD)                | 93.39 (7.23)        |
|                                                | Range                    | 81.6 - 102.0        |
| Body mass index (kg/m <sup>2</sup> )           | Mean (SD)                | 17.77 (1.95)        |
|                                                | Range                    | 15.0 - 19.6         |

Abbreviations: SD = standard deviation; T1D = type 1 diabetes  
Age in years is derived from the age of the participant in months rounded to 1 decimal place. All participants met the inclusion criteria of age <4 years at the time of informed consent and study completion.

Status of Program: Production  
Program Location: /cvn/projects/prj/ecb/programs/000000214172/dev/tables/t\_idm.sas  
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| Population: Safety      |           | 3 mg nasal glucagon |
|-------------------------|-----------|---------------------|
| Duration of T1D (years) | Mean (SD) | 1.36 (0.67)         |
|                         | Range     | 0.7 - 2.5           |

Abbreviations: SD = standard deviation; T1D = type 1 diabetes

Status of Program: Production  
Program Location: /cvn/projects/prj/ecb/programs/000000214172/dev/tables/t\_idm.sas  
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### Prior, Concomitant, and Post-intervention Therapy

Per the inclusion requirements of the study, all participants were receiving insulin therapy by either multiple daily injections or continuous subcutaneous insulin infusion.

### **Treatments**

NG is a drug-device combination product containing 3 mg glucagon powder for nasal delivery.

The same drug-device combination product that is approved for use in adults, adolescents, and children aged 4 years and older was used in this study.

Participants were administered a single dose of 3 mg NG powder.

### **Objective(s)**

#### **Objectives and Endpoints**

| Objectives                                                                                                | Endpoints                                                                                                                                                                              |
|-----------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Primary                                                                                                   |                                                                                                                                                                                        |
| To assess the safety and tolerability of a single dose of NG 3 mg in children aged 1 to <4 years with T1D | Incidence of TEAEs                                                                                                                                                                     |
| Secondary                                                                                                 |                                                                                                                                                                                        |
| To assess the PD of a single dose of NG 3 mg in children aged 1 to <4 years with T1D                      | Change from baseline (predose BG) of maximum BG. Other BG parameters: <ul style="list-style-type: none"> <li>• BG<sub>max</sub></li> <li>• AUC</li> <li>• TBG<sub>max</sub></li> </ul> |
| To assess the PK of a single dose of NG 3 mg in children aged 1 to <4 years with T1D                      | Model-estimated population PK parameters                                                                                                                                               |
| Exploratory                                                                                               |                                                                                                                                                                                        |
| To assess the efficacy of a single dose of NG 3 mg in children aged 1 to <4 years with T1D                | The proportion of participants achieving treatment success defined as an increase of BG $\geq 20$ mg/dL (1.11 mmol/L) from baseline (predose BG) within 30 min postdose                |

Abbreviations: AUC = area under the concentration-time curve; BG = blood glucose; BG<sub>max</sub> = maximum observed blood glucose; NG = nasal glucagon; PD = pharmacodynamics; PK = pharmacokinetics; T1D = type 1 diabetes; TBG<sub>max</sub> = time of maximum observed blood glucose; TEAE = treatment-emergent adverse event.

### **Sample size**

7 participants enrolled in the study

### **Randomisation and blinding**

This was an open label non-randomized study.

## ***Statistical Methods***

Study I8R-MC-IGBO (IGBO) was a Phase 1, open-label, multi-center study with a primary objective of assessing the safety and tolerability of a single 3 mg dose of nasal glucagon (NG) in pediatric participants aged 1 to <4 years with T1D.

The study comprised a single cohort, with each participant receiving a single dose of 3 mg NG.

## **Results**

### ***Participant flow***

Planned: At least 9 participants with an approximate maximum of 20 were planned to be enrolled so that at least 6 evaluable participants completed the study.

Enrolled, treated, completed, and analyzed: 7 participants.

### ***Efficacy results***

All participants achieved treatment success, with an increase in PG of at least 20 mg/dL (1.11 mmol/L) within the 30-minutes post-dose assessment window.

In individual participants, the actual time to treatment success ranged from 10 to 30 minutes. The mean time to success was 15.6 minutes.

### ***Safety results***

#### Incidence of TEAEs

During the study, a total of 9 TEAEs were reported by 5 of the 7 participants, each considered to be related to NG by the investigator. The TEAEs reported by the 5 participants comprised

- Dyspepsia reported by 1 participant on Day 1, approximately 2 hours post-dose, that resolved after 15 minutes.
- Eye pruritus reported in 1 participant on Day 1, 15 minutes post-dose, that resolved after 31 minutes. One event of post-tussive vomiting was reported on Day 2, approximately 36 hours post-dose for the same participant.
- Epistaxis was reported in 1 participant at 1 minute post-dose, followed by sneezing at 7 minutes post-dose. Both events resolved within 1 minute of onset.
- Nasal discomfort was reported by 1 participant at 1 minute post-dose that resolved after approximately 4 hours. Vomiting and Abdominal discomfort were also reported on Day 1, approximately 1.5 hours post-dose by the same participant. Both events had resolved within 3 hours of onset.
- Nausea was reported by 1 participant on Day 1, approximately 2 hours post-dose, that resolved approximately 20 hours after onset.

#### Severity and resolution of TEAEs

All TEAEs were considered to be mild and resolved spontaneously.

### 2.3.2. Discussion on clinical aspects

Although this was a small open label single arm study with only 7 participants aged 1 to 4 years, the results are in line with the results seen in older subjects.

#### Safety

A single 3-mg dose of NG was well tolerated during the study and safety findings were consistent with previous studies of NG. There were no deaths or other SAEs reported. Each of the 9 TEAEs reported were of mild severity and had resolved spontaneously by the end of the study.

Two participants reported nasal, respiratory, and anosmia TEAEs. Epistaxis and sneezing were reported in 1 participant, each with a duration of 1 minute, and 1 participant reported Nasal discomfort with a duration of approximately 4 hours.

There were no clinically significant findings in vital signs measurements or other observations related to safety during the study.

#### PD

Following dosing with 3 mg NG, the mean BG<sub>max</sub> of 242.1 mg/dL (13.4 mmol/L) was achieved at 55.6 minutes post-dose and represented an increase of 132.4 mg/dL (7.35 mmol/L) from the mean concentration at baseline.

#### PK

Model-predicted glucagon geometric mean AUC was 1560 pg\*hr/mL following administration of 3 mg NG.

#### Efficacy

All participants achieved treatment success, with an increase from baseline in PG of 20 mg/dL (1.11 mmol/L) or greater by 30 minutes post-dose.

MAH intends to submit the same data as part of a type II variation application to extend the indication of Baqsimi in the paediatric population (1 to <4 years) in Q4 2024. Further analysis of these data will be performed at that time.

## 3. CHMP overall conclusion and recommendation

☒ **Fulfilled: No regulatory action required.**