CLINICAL UPDATE

Brand Name	Gvoke™
Generic Name	glucagon
Drug Manufacturer	Xeris Pharmaceuticals, Inc.

Clinical Update

TYPE OF CLINICAL UPDATE

New Formulation

FDA APPROVAL DATE

August 20, 2021

LAUNCH DATE

1st quarter 2022

REVIEW DESIGNATION

Standard

TYPE OF REVIEW

Type 3 - New Dosage Form; New Drug Application (NDA): 212097.

DISPENSING RESTRICTIONS

N/A

Overview

INDICATION(S) FOR USE

Gvoke™ is an antihypoglycemic agent indicated for the treatment of severe hypoglycemia in pediatric and adult patients with diabetes ages 2 years and above.

MECHANISMS OF ACTION

Glucagon increases blood glucose concentration by activating hepatic glucagon receptors, thereby stimulating glycogen breakdown and release of glucose from the liver. Hepatic stores of glycogen are necessary for glucagon to produce an antihypoglycemic effect.

DOSAGE FORM(S) AND STRENGTH(S)

Injection:

- 0.5 mg/0 1 mL single-dose pre-filled HypoPen auto-injector.
- 1 mg/0 2 mL single-dose pre-filled HypoPen auto-injector
- 0.5 mg/0 1 mL single-dose pre-filled syringe.
- 1 mg/0 2 mL single-dose pre-filled syringe.

DOSE & ADMINISTRATION

- The recommended dose for adults and pediatric patients aged 12 years and older is 1 mg.
- The recommended dose for pediatric patients aged 2 to under 12 years of age is weight dependant.
  - For pediatric patients who weigh less than 45 kg, the recommended dose is 0.5 mg Gvoke™.

- For pediatric patients who weigh 45 kg or greater, the recommended dose is 1 mg Gvoke™.
- Administer the injection in the lower abdomen, outer thigh, or outer upper arm.

EFFICACY

Adult Patients Type 1 Diabetes Mellitus

Gvoke™ was evaluated in adult patients aged 18 to 74 years with type 1 diabetes in two multicenter 2-way crossover studies, Study A was double-blinded with 80 patients, and Study B was single-blinded with 81 patients. Both studies involved 2 clinic visits 7 to 28 days apart, with random assignment to receive Gvoke ™ 1 mg during one session and GEK 1 mg during the other. 154 subjects received an injection of Gvoke™, and 157 subjects received an injection of GEK. A total of 152 subjects received both Gvoke™ and GEK.

The efficacy of Gvoke™ was compared to GEK in subjects who were in a state of insulin-induced hypoglycemia via insulin infusion with target plasma glucose less than 50 mg/dL. In Study A, mean plasma glucose at time of glucagon administration was 44.8 mg/dL and 45.2 mg/dL for Gvoke™ and GEK, respectively. In Study B, mean plasma glucose at time of glucagon administration was 47.7 mg/dL and 48.7 mg/dL for Gvoke™ and GEK, respectively. Treatment 'success' was defined as plasma glucose increase from mean value at time of glucagon administration to absolute value greater than 70 mg/dL or relative increase of 20 mg/dL or greater, at 30 minutes after glucagon administration. In a pooled analysis of Study A and Study B, the proportion of patients who achieved treatment 'success' was 98.7 % in the Gvoke™ group and 100% in the GEK group and the comparison between groups met the prespecified non-inferiority margin. A summary of treatment 'success' rates is shown in Table 3. The mean time to treatment 'success' was 13.8 minutes in the Gvoke™ group and 10 minutes in the GEK group.

Table: Adult Patients Meeting Treatment Success in Studies A and B Combined

	Study A (n=80)		Study B (n=81)		Pooled Studies A and B (n=161)[b]	
	GVOKE	GEK	GVOKE	GEK	GVOKE	GEK
Treatment Success-n (%)	76 (97 %)	79 (100%)	76 (100%)	78 (100%)	152 (99%)	157 (100%)
Glucose criteria met- n (%)						
Greater than 70 mg/dL	74 (95%)	79 (100%)	76 (100%)	78 (100%)	150 (97%)	157 (100%)
20 mg/dL or greater increase from baseline	76 (97%)	79 (100%)	76 (100%)	78 (100%)	152 (99%)	157 (100%)

[a] Treatment success is defines as blood glucose greater than 70 mg/dL or an increase of blood glucose by 20 mg/dL or greater from baseline. The efficacy analysis population consisted of all patients who received both doses of the study drug.
[b] Percentage based on number of patients from both studies.

Pediatric Patients with Type 1 Diabetes Mellitus

Gvoke™ was evaluated in a study in 31 pediatric patients with type 1 diabetes mellitus. Patients were administered insulin to induce a plasma glucose of less than 80 mg/dL. Patients ages 2 to under 6 years and 6 to under 12 years of age then received a 0.5 mg dose of Gvoke™. Patients ages 12 and older received a 0.5 mg or 1 mg dose of Gvoke™. All evaluable pediatric patients (30/30) achieved a target glucose increase of at least 25 mg/dL. Following administration, plasma glucose levels over time showed similar glucose responses for patients in each age group.

Table: Pediatric Patients with Type 1 Diabetes Mellitus Plasma Glucose by Age Group

Age Group	GVOKE Dose	Plasma Glucose (mg/dL) Mean (SD)		
		Baseline	30 minutes	Change
2 to under 6 years (n=7)	0.5 mg	68.1 (8.3)	149.6 (15.2)	81.4 (18.3)
6 to under 12 years (n=13)	0.5 mg	71.6 (7.6)	155.8 (26.5)	84.2 (25.3)
12 to under 18 years (n=11)	0.5 mg	75.2(2.1)	128.1(20.46)	52.9(19.88)
	1 mg	74.5(4.84)	129.5 (29.5)	55 (27.3)

SD=standard deviation