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HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use GVOKE safely and effectively. See full prescribing information for GVOKE.

GVOKE (glucagon) injection, for subcutaneous use
Initial U.S. Approval: 1960

----------INDICATIONS AND USAGE----------

GVOKE is an antihypoglycemic agent indicated for the treatment of severe hypoglycemia in pediatric and adult patients with diabetes ages 2 years and above. (1)

----------DOSAGE AND ADMINISTRATION----------

- GVOKE auto-injector and pre-filled syringe are for subcutaneous injection only (2.1)
- The recommended dose for adults and pediatric patients aged 12 years and older is 1 mg (2.2)
- The recommended dose for pediatric patients aged 2 to under 12 years of age is weight dependent: (2.2)
  - 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 GVOKE according to the printed instructions on the foil pouch label, carton, or the Instructions for Use (2.1)
- Visually inspect GVOKE prior to administration. The solution should appear clear and colorless to pale yellow and be free of particles. If the solution is discolored or contains particulate matter, do not use (2.1)
- Administer the injection in the lower abdomen, outer thigh, or outer upper arm (2.1)
- Call for emergency assistance immediately after administering the dose (2.1)
- When the patient has responded to treatment, give oral carbohydrates (2.1)
- Do not attempt to reuse GVOKE. Each GVOKE device contains a single dose of glucagon and cannot be reused (2.1)
- If there has been no response after 15 minutes, an additional weight appropriate dose of GVOKE from a new device may be administered while waiting for emergency assistance (2.1)

----------DOSAGE FORMS AND STRENGTHS----------

Injection:

- 0.5 mg/0.1 mL single-dose pre-filled HypoPen auto-injector (3)
- 1 mg/0.2 mL single-dose pre-filled HypoPen auto-injector (3)
- 0.5 mg/0.1 mL single-dose pre-filled syringe (3)
- 1 mg/0.2 mL single-dose pre-filled syringe (3)

----------CONTRAINDICATIONS----------

- Pheochromocytoma (4)
- Insulinoma (4)
- Known hypersensitivity to glucagon or to any of the excipients (4)

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

- *Substantial Increase in Blood Pressure in Patients Pheochromocytoma:* Contraindicated in patients with pheochromocytoma because GVOKE may stimulate the release of catecholamines from the tumor. (4, 5.1)
- *Hypoglycemia in Patients with Insulinoma:* In patients with insulinoma, administration may produce an initial increase in blood glucose; however, GVOKE may stimulate exaggerated insulin release from an insulinoma and cause hypoglycemia. If a patient develops symptoms of hypoglycemia after a dose of GVOKE, give glucose orally or intravenously. (4, 5.2)
- *Hypersensitivity and Allergic Reactions:* Allergic reactions have been reported and include generalized rash, and in some cases anaphylactic shock with breathing difficulties, and hypotension. (4, 5.3)
- *Lack of Efficacy in Patients with Decreased Hepatic Glycogen*: GVOKE 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 GVOKE to be effective. Patients with these conditions should be treated with glucose. (5.4)
- *Necrolytic Migratory Erythema (NME):* a skin rash, has been reported postmarketing following continuous glucagon infusion and resolved with discontinuation of the glucagon. Should NME occur, consider whether the benefits of continuous glucagon infusion outweigh the risks. (5.5)

----------ADVERSE REACTIONS----------

- Most common adverse reactions (incidence 2% or greater) reported were:
- Adults—nausea, vomiting, injection site edema raised 1 mm or greater, and headache (6.1)
- Pediatric Patients—nausea, hypoglycemia, vomiting, headache, abdominal pain, hyperglycemia, injection site discomfort and reaction, and urticaria (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Xeris Pharmaceuticals at toll-free 1-877-937-4737 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------

- *Beta-blockers:* Patients taking beta-blockers may have a transient increase in pulse and blood pressure. (7.1)
- *Indomethacin:* In patients taking indomethacin GVOKE may lose its ability to raise glucose or may produce hypoglycemia. (7.2)
- *Warfarin:* GVOKE may increase the anticoagulant effect of warfarin. (7.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling including Instructions for Use.

Revised: 07/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

GVOKE is indicated for the treatment of severe hypoglycemia in pediatric and adult patients with diabetes ages 2 years and above.

2 DOSAGE AND ADMINISTRATION

2.1 Important Administration Instructions

GVOKE auto-injector and pre-filled syringe are for subcutaneous injection only.

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 GVOKE and its Instructions for Use. Administer GVOKE as soon as possible when severe hypoglycemia is recognized.

Instruct the patient or caregiver to read the Instructions for Use at the time they receive a prescription for GVOKE. Emphasize the following instructions to the patient or caregiver:

- Do not open foil pouch until ready to administer GVOKE.
- Administer GVOKE according to the printed instructions on the foil pouch label, carton, or the Instructions for Use.
- Visually inspect GVOKE prior to administration. The solution should appear clear and colorless to pale yellow and be free of particles. If the solution is discolored or contains particulate matter, do not use.
- Administer the injection in the lower abdomen, outer thigh, or outer upper arm.
- Call for emergency assistance immediately after administering the dose.
- If there has been no response after 15 minutes, an additional dose from a new device may be administered while waiting for emergency assistance.
- When the patient has responded to treatment, give oral carbohydrates to restore the liver glycogen and prevent recurrence of hypoglycemia.
- Do not attempt to reuse GVOKE. Each GVOKE device contains a single dose of glucagon and cannot be reused.

2.2 Dosage in Adults and Pediatric Patients Aged 2 years and Above

Adults and Pediatric Patients Aged 12 and Older

- The recommended dose of GVOKE is 1 mg administered by subcutaneous injection into lower abdomen, outer thigh, or outer upper arm.
- If there has been no response after 15 minutes, an additional 1 mg dose of GVOKE from a new device may be administered while waiting for emergency assistance.

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Pediatric Patients Aged 2 to Under 12 Years of Age

- The recommended dose for pediatric patients who weigh less than 45 kg is 0.5 mg GVOKE administered by subcutaneous injection into the lower abdomen, outer thigh, or outer upper arm.
- The recommended dose for pediatric patients who weigh 45 kg or greater is 1 mg GVOKE administered by subcutaneous injection into the lower abdomen, outer thigh, or outer upper arm.
- If there has been no response after 15 minutes, an additional weight appropriate dose of GVOKE from a new device may be administered while waiting for emergency assistance.

3 DOSAGE FORMS AND STRENGTHS

GVOKE injection is a clear, colorless to pale yellow solution available as follows:

- 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

4 CONTRAINDICATIONS

GVOKE is contraindicated in patients with:

- Pheochromocytoma because of the risk of substantial increase in blood pressure *[see Warnings and Precautions (5.1)]*
- Insulinoma because of the risk of hypoglycemia *[see Warnings and Precautions (5.2)]*
- Known hypersensitivity to glucagon or to any of the excipients in GVOKE. Allergic reactions have been reported with glucagon and include anaphylactic shock with breathing difficulties and hypotension *[see Warnings and Precautions (5.3)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Substantial Increase in Blood Pressure in Patients Pheochromocytoma

GVOKE is contraindicated in patients with pheochromocytoma because glucagon may stimulate the release of catecholamines from the tumor *[see Contraindications (4)]*. If the patient develops a substantial increase in blood pressure and a previously undiagnosed pheochromocytoma is suspected, 5 to 10 mg of phentolamine mesylate, administered intravenously, has been shown to be effective in lowering blood pressure.

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5.2 Hypoglycemia in Patients with Insulinoma

In patients with insulinoma, administration of glucagon may produce an initial increase in blood glucose; however, GVOKE administration may directly or indirectly (through an initial rise in blood glucose) stimulate exaggerated insulin release from an insulinoma and cause hypoglycemia. GVOKE is contraindicated in patients with insulinoma *[see Contraindications (4)]*. If a patient develops symptoms of hypoglycemia after a dose of GVOKE, give glucose orally or intravenously.

5.3 Hypersensitivity and Allergic Reactions

Allergic reactions have been reported with glucagon, these include generalized rash, and in some cases anaphylactic shock with breathing difficulties and hypotension. GVOKE is contraindicated in patients with a prior hypersensitivity reaction *[see Contraindications (4)]*.

5.4 Lack of Efficacy in Patients with Decreased Hepatic Glycogen

GVOKE 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 GVOKE administration to be effective. Patients with these conditions should be treated with glucose.

5.5 Necrolytic Migratory Erythema

Necrolytic migratory erythema (NME), a skin rash commonly associated with glucagonomas (glucagon-producing tumors) and characterized by scaly, pruritic erythematous plaques, bullae, and erosions, has been reported postmarketing following continuous glucagon infusion. NME lesions may affect the face, groin, perineum and legs or be more widespread. In the reported cases NME resolved with discontinuation of the glucagon, and treatment with corticosteroids was not effective. Should NME occur, consider whether the benefits of continuous glucagon infusion outweigh the risks.

6 ADVERSE REACTIONS

The following serious adverse reactions are described below and elsewhere in labeling:

- Hypersensitivity and Allergic Reactions *[see Warnings and Precautions (5.3)]*.
- Necrolytic Migratory Erythema *[see Warnings and Precautions (5.5)]*.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of GVOKE cannot be directly compared to rates in the clinical trials of other drugs and may not reflect the rates observed in practice.

Adverse Reactions in Adult Patients

The safety of GVOKE was evaluated in two randomized, blinded, 2-way crossover studies conducted in adults with type 1 diabetes mellitus. In total, 154 patients received an injection of GVOKE *[see Clinical Studies (14.1)]*.

The most common adverse reactions occurring in 2% or more of adult subjects treated with GVOKE during clinical trials are listed in Table 1.

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Table 1: Adverse Reactions Occurring ≥ 2% in Adult Patients with Type 1 Diabetes Mellitus Treated with GVOKE[a]

	GVOKE 1 mg dose (N = 154)
Nausea	30%
Vomiting	16%
Injection site edema raised 1 mm or greater	7%
Headache	5%

[a]Adverse Reactions occurring within 12 hours.

Injection site pain was reported by 1% of patients with GVOKE.

Hypertension and tachycardia have occurred with glucagon treatment.

Adverse Reactions in Pediatric Patients Aged 2 Years and Older

The safety of GVOKE was evaluated in one single-arm, open-label, study in 31 pediatric patients with type 1 diabetes mellitus *[see Clinical Studies (14.2)]*.

The data in Table 2 reflect the exposure of 31 pediatric patients to 0.5 mg or 1 mg of GVOKE. The most common adverse reactions occurring in 2% or greater of pediatric patients treated with GVOKE are listed in Table 2.

Table 2: Adverse Reactions Occuring ≥ 2% in Pediatric Patients with Type 1 Diabetes Treated with GVOKE[a]

	Ages 2 to under 6 years of age (0.5 mg dose) N =7	Ages 6 to under 12 years of age (0.5 mg dose) N = 13	Ages 12 to under 18 (1 mg dose) N = 11	Total N = 31
Nausea	43%	54%	36%	45%
Hypoglycemia	29%	54%	27%	39%
Vomiting	14%	23%	18%	19%
Headache	0%	15%	0%	7%
Abdominal pain	0%	8%	0%	3%
Hyperglycemia	14%	8%	0%	7%
Injection site discomfort	0%	8%	0%	3%

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	Ages 2 to under 6 years of age (0.5 mg dose) N =7	Ages 6 to under 12 years of age (0.5 mg dose) N = 13	Ages 12 to under 18 (1 mg dose) N = 11	Total N = 31
Injection site reaction	0%	0%	9%	3%
Urticaria	0%	8%	0%	3%

[a]Adverse Reactions occurring within 12 hours.

6.2 Postmarketing Experience

Additional adverse reactions have been identified during post-approval use of glucagon. Because these reactions are reported voluntarily from a population of uncertain size, it is generally not possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

- Necrolytic migratory erythema (NME) cases have been reported postmarketing in patients receiving continuous infusion of glucagon.
- Hypoglycemia and hypoglycemic coma. Patients taking indomethacin may be more likely to experience hypoglycemia following glucagon administration *[see Drug Interactions (7)]*.

7 DRUG INTERACTIONS

7.1 Beta-Blockers

Patients taking beta-blockers may have a transient increase in pulse and blood pressure when given GVOKE.

7.2 Indomethacin

In patients taking indomethacin, GVOKE may lose its ability to raise blood glucose or may even produce hypoglycemia.

7.3 Warfarin

GVOKE may increase the anticoagulant effect of warfarin.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Available data from case reports and a small number of observational studies with glucagon use in pregnant women over decades of use have not identified a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. Multiple small studies have demonstrated a lack of transfer of pancreatic glucagon across the human placental barrier during early gestation. In a rat reproduction study, no embryofetal toxicity was observed with glucagon

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administered by injection during the period of organogenesis at doses representing up to 40 times the human dose, based on body surface area (mg/m^2) *(see Data)*.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data

Animal Data

In pregnant rats given animal sourced glucagon twice-daily by injection at doses up to 2 mg/kg (up to 40 times the human dose based on body surface area extrapolation, mg/m^2) during the period of organogenesis, there was no evidence of increased malformations or embryofetal lethality.

8.2 Lactation

Risk Summary

There is no information available on the presence of glucagon in human or animal milk, the effects of the drug on the breastfed infant, or the effects of the drug on milk production. However, glucagon is a peptide and would be expected to be broken down to its constituent amino acids in the infant's digestive tract and is therefore, unlikely to cause harm to an exposed infant.

8.4 Pediatric Use

The safety and effectiveness of GVOKE for the treatment of severe hypoglycemia in patients with diabetes have been established in pediatric patients ages 2 years and above. Use of GVOKE for this indication is supported by evidence from a study in 31 pediatric patients ages 2 and older with type 1 diabetes mellitus *[see Clinical Studies (14.2)*].

The safety and effectiveness of GVOKE have not been established in pediatric patients younger than 2 years of age.

8.5 Geriatric Use

Clinical studies of GVOKE did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Limited clinical trial experience has not identified differences in responses between the elderly and younger patients.

10 OVERDOSAGE

If overdosage occurs, the patient may experience nausea, vomiting, inhibition of GI tract motility, increase in blood pressure, and pulse rate. In case of suspected overdosing, serum potassium may decrease and should be monitored and corrected if needed. If the patient develops a dramatic increase in blood pressure, phentolamine mesylate has been shown to be effective in lowering blood pressure for the short time that control would be needed.

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11 DESCRIPTION

GVOKE contains glucagon, an antihypoglycemic agent used to treat severe hypoglycemia. Glucagon is a single chain containing 29 amino acid residues and has a molecular weight of 3483 and is identical to human glucagon. Glucagon is produced by solid phase synthesis with subsequent purification.

Its molecular formula is $C_{153}H_{225}N_{43}O_{49}S$ with the following structure:

GVOKE is a clear, colorless to pale yellow, sterile solution for subcutaneous injection available in 0.5 mg per 0.1 mL or 1 mg per 0.2 mL auto-injector or pre-filled syringe.

Each 0.2 mL of GVOKE contains 1 mg of glucagon, 11.1 mg of trehalose dihydrate NF, and 1.2 mg of 1N sulfuric acid NF, in dimethyl sulfoxide diluent.

Each 0.1 mL of GVOKE contains 0.5 mg of glucagon, 5.6 mg of trehalose dihydrate NF, and 0.6 mg of 1N sulfuric acid NF, in dimethyl sulfoxide diluent.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism 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.

12.2 Pharmacodynamics

After administration of 1 mg GVOKE in adult patients with diabetes, the mean maximum glucose increase from baseline was 176 mg/dL.

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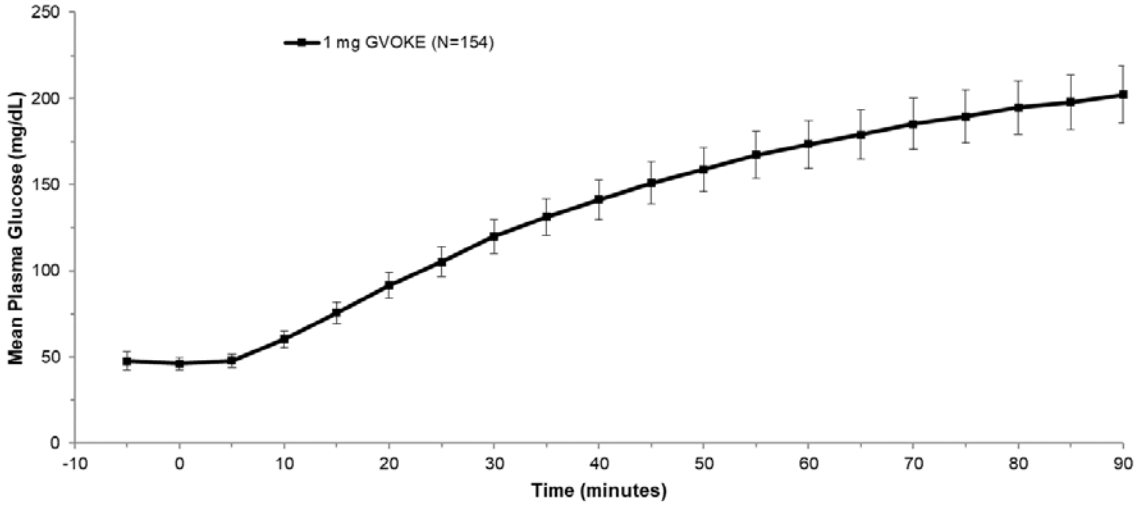
Figure 1: Mean ± Standard Error of the Mean (SEM) Plasma Glucose vs. Time from 1 mg GVOKE Injection in Adult Subjects with Type 1 Diabetes Mellitus



In pediatric patients with type 1 diabetes (2 to less than 18 years), the mean maximum glucose increase from baseline was 134 mg/dL (2 to less than 6 years), 145 mg/dL (6 to less than 12 years), and 123 mg/dL (12 to less than 18 years).

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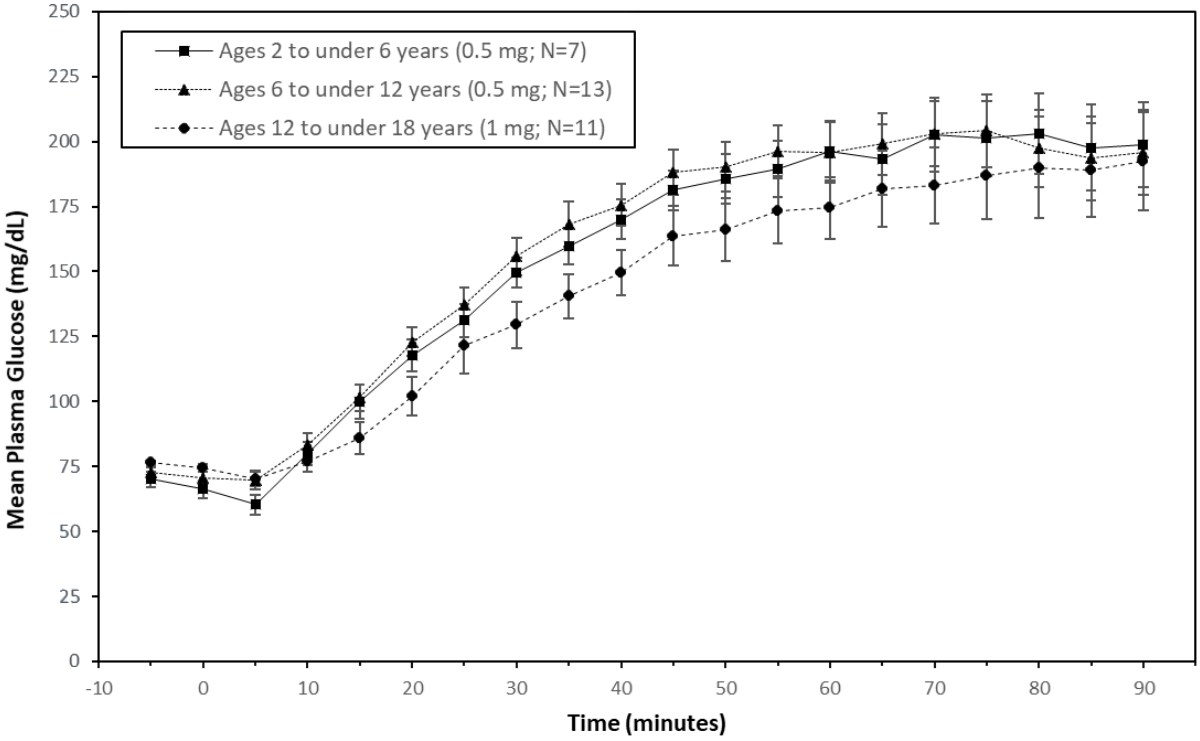
Figure 2: Mean (± SEM) Plasma Glucose vs. Time from GVOKE Injection in Pediatric Subjects with Type 1 Diabetes Mellitus



12.3 Pharmacokinetics

Absorption

Subcutaneous injection of 1 mg GVOKE in adult type 1 diabetes mellitus subjects resulted in a mean glucagon C_{max} of 2481.3 pg/mL, t_{max} of 50 minutes and $AUC_{0\text{-}240min}$ of 3454.6 pg*min/mL.

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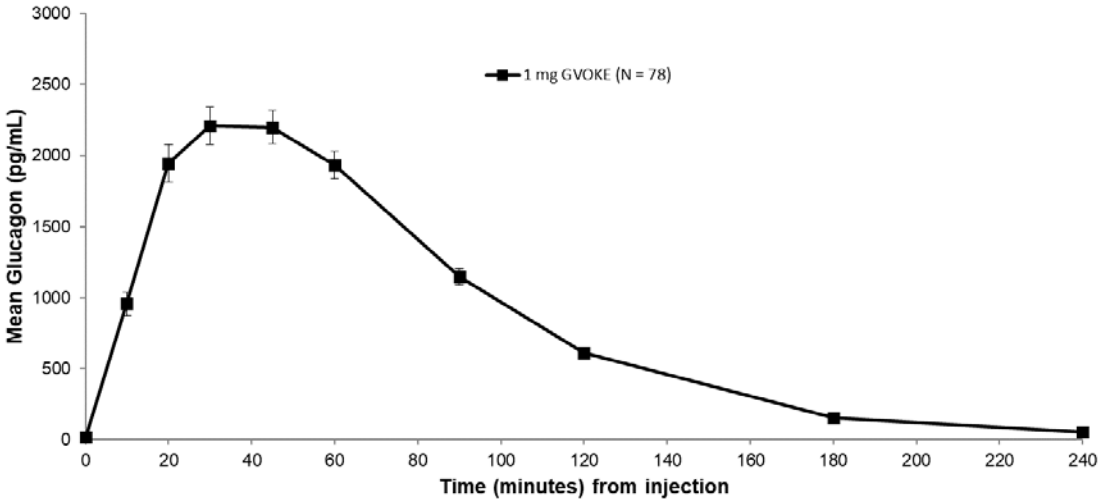
Figure 3: Mean (± SEM) Plasma Glucagon Concentration vs. Time for 1 mg GVOKE Injection in Adults with Type 1 Diabetes Mellitus



Distribution

The apparent volume of distribution was in the range of 137-2425 L.

Elimination

The half-life of GVOKE was determined to be 32 minutes.

Metabolism

Glucagon is extensively degraded in liver, kidney, and plasma.

Excretion

Urinary excretion of intact glucagon has not been measured.

Specific Populations

Pediatrics

Subcutaneous injection of 0.5 mg GVOKE in subjects ages 2 to under 6 years resulted in a mean glucagon C_{max} of 2300 pg/mL, t_{max} of 41 minutes, and $AUC_{0\text{-}180min}$ of 138900 pg/mL*min. Subcutaneous injection of 0.5 mg GVOKE in subjects ages 6 to under 12 years resulted in a mean C_{max} of 1600 pg/mL, median t_{max} of 34 minutes and $AUC_{0\text{-}180min}$ of 104700 pg/mL*min. Subcutaneous injection of 1 mg GVOKE in subjects ages 12 to less than 18 years resulted in a mean C_{max} of 1900 pg/mL, t_{max} of 51 minutes $AUC_{0\text{-}180min}$ of 134300 pg/mL*min. Mean plasma glucagon levels were similar across the age groups following age appropriate doses of GVOKE.

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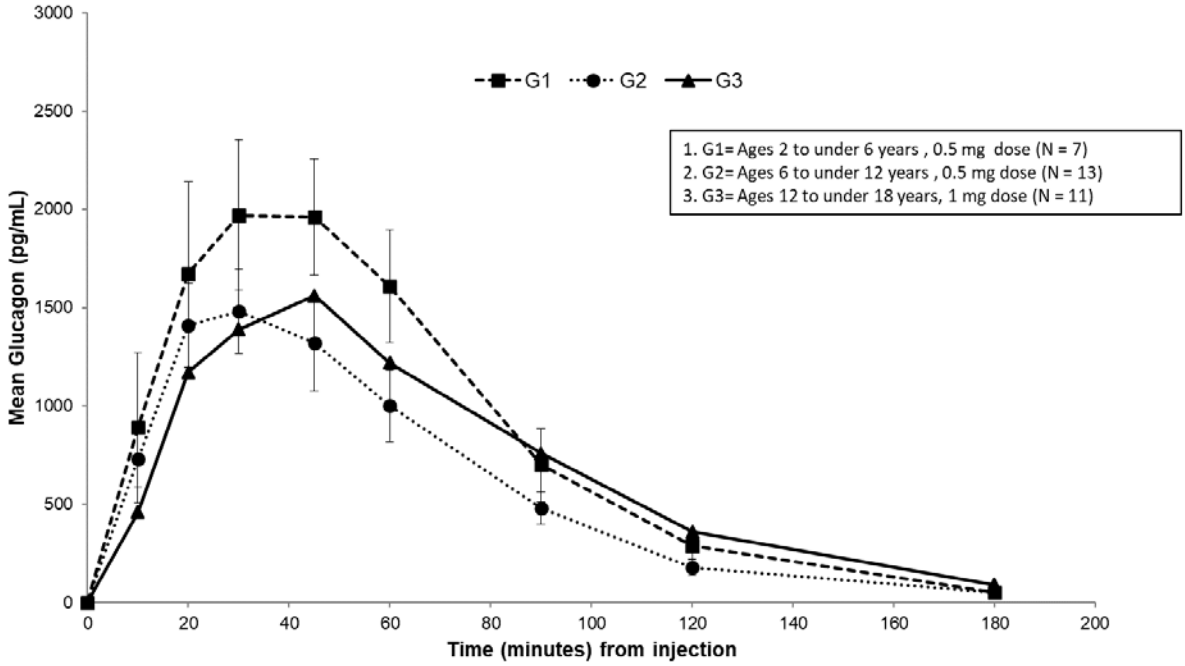
Figure 4: Mean (± SEM) Plasma Glucagon Concentration vs. Time from GVOKE Injection in Pediatric Patients with Type 1 Diabetes Mellitus



13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long term studies in animals to evaluate carcinogenic potential have not been performed. Recombinant glucagon was positive in the bacterial Ames assay. It was determined that an increase in colony counts was related to technical difficulties in running this assay with peptides. Studies in rats have shown that glucagon does not cause impaired fertility.

14 CLINICAL STUDIES

14.1 Adult Patients Type 1 Diabetes Mellitus

GVOKE was evaluated in adult patients aged 18 to 74 years with type 1 diabetes in two multi-center 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

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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 pre-specified 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 3: 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 (%)[a]	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.

14.2 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. A summary of plasma glucose results are shown in Table 4.

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Table 4: 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

16 HOW SUPPLIED/STORAGE AND HANDLING

GVOKE injection is supplied as a clear, colorless to pale yellow solution in the following configurations:

GVOKE	Strength	Package Size	NDC number
HypoPen	0.5 mg per 0.1 mL	1 single-dose auto-injector	72065-120-11
HypoPen	0.5 mg per 0.1 mL	2 single-dose auto-injectors	72065-120-12
HypoPen	1 mg per 0.2 mL	1 single-dose auto-injector	72065-121-11
HypoPen	1 mg per 0.2 mL	2 single-dose auto-injectors	72065-121-12
PFS	0.5 mg per 0.1 mL	1 single-dose pre-filled syringe	72065-130-11
PFS	0.5 mg per 0.1 mL	2 single-dose pre-filled syringes	72065-130-12
PFS	1 mg per 0.2 mL	1 single-dose pre-filled syringe	72065-131-11
PFS	1 mg per 0.2 mL	2 single-dose pre-filled syringes	72065-131-12

- Store GVOKE at 20° to 25°C (68° to 77°F); excursions permitted between 15° and 30°C (59° and 86°F). Do not refrigerate or freeze. Do not expose to extreme temperatures.
- Store the GVOKE HypoPen and pre-filled syringe in the original sealed foil pouch until time of use.

17 PATIENT COUNSELING INFORMATION

Advise the patient and family members or caregivers to read the FDA-approved patient labeling (Instructions for Use).

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Recognition of Severe Hypoglycemia

Inform patient and family members or caregivers on how to recognize the signs and symptoms of severe hypoglycemia and the risks of prolonged hypoglycemia.

Administration

Review the Patient Information and Instructions for Use with the patient and family members or caregivers.

Serious Hypersensitivity

Inform patients that allergic reactions can occur with GVOKE. Advise patients to seek immediate medical attention if they experience any symptoms of serious hypersensitivity reactions [*see Warnings and Precautions (5.3)*].

GVOKE® is a trademark of Xeris Pharmaceuticals, Inc.

Manufactured for Xeris Pharmaceuticals, Inc. by Pyramid Laboratories Inc., Costa Mesa, CA 92626

For information contact:

Xeris Pharmaceuticals, Inc.

180 North LaSalle Street, Suite 1600, Chicago, IL 60601

1-877-XERIS-37 (1-877-937-4737)

www.xerispharma.com

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