

Summary of Instructions for Use

GlucaGen[®] HypoKit[®] (glucagon [rDNA origin] for injection)

This is only a summary of the Instructions for Use. Please see the full Instructions for Use on the following pages.

Preparing the GlucaGen[®] dose



Step 1. Check that the orange plastic cap on your vial of GlucaGen[®] is firmly attached. **Do not** use if the cap is loose or missing. With your thumb, flip the cap off the GlucaGen[®] vial.



Step 4. Hold the vial and syringe together, with the needle still inserted into the vial. Carefully turn the vial and syringe together right side up. Slowly push the plunger down until the syringe is empty. **Do not take the syringe out of the vial.**



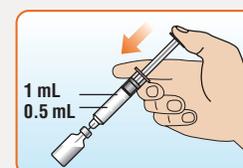
Step 7. Keep the needle inside the vial. Check the syringe for air bubbles. If you see bubbles, tap the syringe until the bubbles rise to the top of the syringe. Gently push on the plunger to move only the air bubbles back into the vial.



Step 2. Pick up the prefilled syringe containing sterile water. **Do not use any other liquid to mix the medicine.** Hold the syringe with 1 hand. With your other hand, pull the needle cover off the syringe. **Do not** remove the plastic backstop from the syringe.



Step 5. Firmly hold both the vial and syringe together in one hand, and gently shake until the powder is completely dissolved. Do not use if a gel has formed, or if you see particles in the solution. **Do not take the syringe out of the vial.**



Step 8. Hold the vial and syringe as shown.

- The usual dose for adults and children who weigh more than 55 pounds (25 kg) is 1 mg (1 mL). Use the content of the full syringe (1 mL).
- The usual dose for children who weigh less than 55 pounds (25 kg) is 0.5 mg (0.5 mL). Gently push the plunger until it is at the 0.5 mL mark on the syringe to ensure there is 0.5 mL liquid left in the syringe.



Step 3. Pick up the GlucaGen[®] vial of dry powder. Hold the vial with 1 hand. With your other hand, push the needle of the prefilled syringe through the center of the rubber stopper.



Step 6. With the needle still inserted into the vial, carefully turn the vial and syringe together upside down. Gently pull down on the plunger and slowly withdraw all of the liquid into the syringe. Do not pull the plunger out of the syringe.

Take the syringe and needle out of the vial when the correct dose of GlucaGen[®] is in the syringe.

If you do not know how much the child weighs:

- Give a child under 6 years of age 0.5 mg (0.5 mL).
- Give a child 6 years of age and older 1 mg (1 mL).

See instructions for giving the injection on the next page ►

Indications and Usage

What is GlucaGen[®] (glucagon [rDNA origin] for injection) HypoKit[®]?

GlucaGen[®] HypoKit[®] is a prescription medicine used to treat very low blood sugar (severe hypoglycemia) in people with diabetes who use insulin.

Important Safety Information

Who should not use GlucaGen[®] HypoKit[®]?

Do not use GlucaGen[®] HypoKit[®] if:

- you are allergic to glucagon or lactose or any of the ingredients in GlucaGen[®] HypoKit[®]
- you have a tumor in the gland on top of your kidneys (adrenal gland) called a pheochromocytoma

- you have a tumor of the pancreas called an insulinoma

What should I tell my doctor before using GlucaGen[®] HypoKit[®]?

Before using GlucaGen[®] HypoKit[®], tell your doctor about all of your medical conditions, including if you:

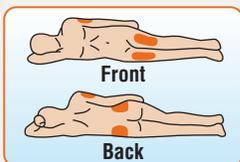
- have kidney problems
- have pancreas problems. Tumors in your pancreas called glucagonomas
- have not had food or water for a long time (prolonged fasting or starvation)
- have low blood sugar that does not go away (chronic hypoglycemia)
- have heart problems

- are pregnant, plan to become pregnant, are breastfeeding, or plan to breastfeed. It is not known if GlucaGen[®] HypoKit[®] passes into your breast milk

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins and herbal supplements. GlucaGen[®] HypoKit[®] may affect the way other medicines work, and other medicines may affect how GlucaGen[®] HypoKit[®] works.

Please see additional Important Safety Information on next page, and Prescribing Information on following pages.

Giving the GlucaGen® injection

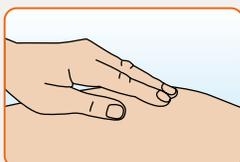


Step 9. Choose the injection site. Common injection sites for GlucaGen® are upper arms, thighs, or buttocks.



Step 10. With one hand gently pinch the skin at the injection site. With your other hand insert the needle into the skin and push the plunger down until the syringe is empty.

After Giving the GlucaGen® injection



Step 11. Pull the needle out of the skin and press on the injection site. Throw away your used syringe with the needle attached and any GlucaGen® you did not use. See **“How should I dispose of (throw away) used GlucaGen® prefilled syringes”** in the full Instructions for Use on the following pages.

Step 12. Turn the person on their side. When an unconscious person awakens, they may vomit. Turning the person on their side will lessen the chance of choking.

Step 13. Call for emergency medical help right away.

Step 14. Feed the person as soon as they are awake and able to swallow.

Give the person a fast-acting source of sugar (such as a regular soft drink or fruit juice) and a long-acting source of sugar (such as crackers and cheese or a meat sandwich).

Step 15. Even if the GlucaGen® treatment wakes the person, tell their doctor right away. The doctor should be told whenever a severe drop in blood sugar (hypoglycemia reaction) happens. The person's dose of diabetes medicine may need to be changed.

Hypoglycemia may happen again after receiving GlucaGen® treatment.

Early symptoms of hypoglycemia may include: sweating, drowsiness, dizziness, sleep disturbances, irregular heartbeat (palpitation), anxiety, tremor, blurred vision, hunger, slurred speech, depressed mood, tingling in the hands, feet, lips, or tongue, irritability, abnormal behavior, lightheadedness, unsteady movement, inability to concentrate, personality changes, headache, and restlessness.

If not treated early, hypoglycemia may worsen and the person may have severe hypoglycemia.

Signs of severe hypoglycemia include: confusion, unconsciousness, seizures, and death.

Important Safety Information (cont'd)

How should I use GlucaGen® HypoKit®?

- Read the detailed **Instructions for Use** that come with GlucaGen® HypoKit®.
- Use GlucaGen® HypoKit® exactly as your doctor tells you to.
- Make sure that you and your family know how to use GlucaGen® HypoKit® the right way before you need it.
- Act quickly. Having low blood sugar for a period of time may be harmful.
- **Call for emergency medical help right after you use GlucaGen® HypoKit®.**
- Eat sugar or a sugar-sweetened product such as a regular soft drink or fruit juice as soon as you are able to swallow.
- Tell your doctor each time you use GlucaGen® HypoKit®. Your doctor may need to change the dose of your diabetes medicines.

What should I avoid while using GlucaGen® HypoKit®?

While using GlucaGen® HypoKit® do not:

- drive or operate machinery until you have eaten sugar or a sugar-sweetened product such as a regular soft drink or fruit juice.

What are the possible side effects of GlucaGen® HypoKit®?

GlucaGen® HypoKit® may cause serious side effects, including:

- **High blood pressure.** High blood pressure is common after taking GlucaGen® HypoKit® and can be severe.
- **Low blood sugar.** GlucaGen® HypoKit® can cause low blood sugar in patients with tumors in their pancreas called insulinomas and glucagonomas by making too much insulin in their bodies.
- **Allergic reactions.** Symptoms of a serious allergic reaction to GlucaGen® HypoKit® may include rash, difficulty breathing, or low blood pressure (hypotension).

The most common side effects of GlucaGen® HypoKit® include nausea, vomiting, temporary fast heartbeat or pounding in your chest (tachycardia).

Tell your doctor if you have any side effect that bothers you or that does not go away.

Please see additional Important Safety Information on previous page, and Prescribing Information on following pages.

GlucaGen® HypoKit® is available by prescription only.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

If you need assistance with prescription costs, help may be available. Visit pparx.org or call 1-888-4PPA-NOW.



GlucaGen® and HypoKit® are registered trademarks of Novo Nordisk A/S. Novo Nordisk is a registered trademark of Novo Nordisk A/S.

© 2017 Novo Nordisk All rights reserved. USA17INP01421 June 2017

GlucaGen® HypoKit®
(glucagon [rDNA origin] for injection)

GlucaGen[®]

(glucagon [rDNA origin] for injection)

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use GlucaGen[®] safely and effectively. See full prescribing information for GlucaGen[®].

GlucaGen[®] (glucagon [rDNA origin] for injection)

Initial U.S. Approval: 1998

RECENT MAJOR CHANGES

Dosage and Administration, Treatment of severe hypoglycemia (2.1) 12/2015

INDICATIONS AND USAGE

GlucaGen[®] is an antihypoglycemic agent and a gastrointestinal motility inhibitor indicated for:

- Treatment of severe hypoglycemia (1.1)
- Use as a diagnostic aid (1.2)

DOSAGE AND ADMINISTRATION

Treatment of severe hypoglycemia (GlucaGen[®] HypoKit[®])

- Reconstitute before administration. (2.1)
- Inject 1 mL (adults and children, weighing more than 55 lbs (25 kg)) or 0.5 mL (children weighing less than 55 lbs (25 kg)) subcutaneously, intramuscularly, or intravenously. (2.1)
- If the weight is not known: Children younger than 6 years should be given 0.5 mL and children 6 years and older should be given 1 mL. (2.1)
- Seek emergency assistance immediately after subcutaneous or intramuscular injection of glucagon. Glucagon injection may be repeated while waiting for emergency assistance. (2.1)
- Intravenous glucose MUST be administered if the patient fails to respond to glucagon. (2.1)
- When the patient responds to treatment, give oral carbohydrates to restore the liver glycogen and prevent recurrence of hypoglycemia. (2.1)

Use as a diagnostic aid (GlucaGen[®] Diagnostic Kit and GlucaGen[®] 10-Pack)

- Reconstitute before administration. (2.2)
- The dose ranges from 0.2 mg to 2 mg depending on the diagnostic technique and the route of administration. (2.2)
- After the end of the diagnostic procedure, give oral carbohydrates to patients who have been fasting, if this is compatible with the diagnostic procedure applied. (2.2)

DOSAGE FORMS AND STRENGTHS

- Each vial contains 1 mg/mL (1 unit/mL) GlucaGen[®] when reconstituted with Sterile Water for Reconstitution or Sterile Water for Injection, USP. (3)

CONTRAINDICATIONS

- Do not use in patients with known hypersensitivity to glucagon or lactose (4)
- Do not use in patients with pheochromocytoma (4)
- Do not use in patients with insulinoma (4)

WARNINGS AND PRECAUTIONS

- Administer cautiously to patients suspected of having glucagonoma due to risk of secondary hypoglycemia. Glucagon may release catecholamines from pheochromocytomas and is contraindicated in patients with this condition. (5.1, 5.2)
- Allergic reactions may occur and include generalized rash, and in rare cases anaphylactic shock with breathing difficulties, and hypotension. (5.3)
- In order for GlucaGen[®] treatment to reverse hypoglycemia, there must be adequate amounts of glycogen stored in the liver. GlucaGen[®] should be used with caution in patients with conditions resulting in low levels of releasable glucose in the liver. (5.4)
- Use caution when glucagon is used as a diagnostic aid in diabetic patients because it may cause hyperglycemia. (5.4)
- Use with caution in patients with known cardiac disease, as glucagon increases myocardial oxygen demand. (5.5)

ADVERSE REACTIONS

Adverse reactions seen with GlucaGen[®] are:

- Nausea and vomiting (6)
- Temporary increase in blood pressure and pulse may occur after administration. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Novo Nordisk Inc. at 1-800-727-6500 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Beta-blockers may cause a greater increase in both pulse and blood pressure after administration. (7.1)
- Glucagon may lose its ability to raise blood glucose or may produce hypoglycemia when given with indomethacin. (7.2)
- Coadministration with an anticholinergic drug is not recommended due to increased gastrointestinal side effects. (7.3)
- Glucagon may increase the anticoagulant effect of warfarin. (7.4)
- Insulin reacts antagonistically towards glucagon. (7.5)

USE IN SPECIFIC POPULATIONS

- Nursing mothers: unknown whether drug is excreted in human milk, therefore caution should be exercised. (8.3)
- Pediatrics: reported safe and effective for treatment of hypoglycemia. Safety and effectiveness for use as a diagnostic aid have not been established. (8.4)

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

Revised: 12/2015

FULL PRESCRIBING INFORMATION: CONTENTS*

1	INDICATIONS AND USAGE	6	ADVERSE REACTIONS	13	NONCLINICAL TOXICOLOGY
1.1	Treatment of severe hypoglycemia	7	DRUG INTERACTIONS	13.1	Carcinogenesis, Mutagenesis, Impairment of Fertility
1.2	Use as a diagnostic aid	7.1	Beta-blockers	16	HOW SUPPLIED/STORAGE AND HANDLING
2	DOSAGE AND ADMINISTRATION	7.2	Indomethacin	16.1	How Supplied
2.1	Treatment of severe hypoglycemia	7.3	Anticholinergic Drugs	16.2	Recommended Storage
2.2	Use as a diagnostic aid	7.4	Warfarin	17	PATIENT COUNSELING INFORMATION
3	DOSAGE FORMS AND STRENGTHS	7.5	Insulin	17.1	Physician Instructions
4	CONTRAINDICATIONS	8	USE IN SPECIFIC POPULATIONS	*Sections or subsections omitted from the full prescribing information are not listed.	
5	WARNINGS AND PRECAUTIONS	8.1	Pregnancy		
5.1	Pheochromocytoma	8.3	Nursing Mothers		
5.2	Insulinoma and Glucagonoma	8.4	Pediatric Use		
5.3	Hypersensitivity and Allergic Reactions	10	OVERDOSAGE		
5.4	Glycogen Stores and Hypoglycemia	11	DESCRIPTION		
5.5	Cardiac Disease	12	CLINICAL PHARMACOLOGY		
5.6	Laboratory Tests	12.1	Mechanism of Action		
		12.2	Pharmacodynamics		
		12.3	Pharmacokinetics		

FULL PRESCRIBING INFORMATION**1 INDICATIONS AND USAGE****1.1 Treatment of severe hypoglycemia**

GlucaGen® is used to treat severe hypoglycemic (low blood sugar) reactions which may occur in patients with diabetes mellitus treated with insulin. Because GlucaGen® depletes glycogen stores, the patient should be given supplemental carbohydrates as soon as he/she awakens and is able to swallow, especially children or adolescents. Medical evaluation is recommended for all patients who experience severe hypoglycemia.

1.2 Use as a diagnostic aid

GlucaGen® is indicated for use during radiologic examinations to temporarily inhibit movement of the gastrointestinal tract. Glucagon is as effective for this examination as are the anticholinergic drugs. However, the addition of the anticholinergic agent may result in increased side effects. After the end of the diagnostic procedure, give oral carbohydrates to patients who have been fasting, if this is compatible with the diagnostic procedure applied.

2 DOSAGE AND ADMINISTRATION**For GlucaGen® HypoKit®:****2.1 Treatment of severe hypoglycemia**

- Using the supplied prefilled syringe, carefully insert the needle through the rubber stopper of the vial containing GlucaGen® powder and inject all the liquid from the syringe into the vial.
- Shake the vial gently until the powder is completely dissolved and no particles remain in the fluid. The reconstituted fluid should be clear and of water-like consistency.
- The reconstituted GlucaGen® gives a concentration of approximately 1 mg/mL glucagon.
- The reconstituted GlucaGen® should be used immediately after reconstitution.
- Inject 1 mL (adults and children, weighing more than 55 lbs (25 kg)) or 0.5 mL (children weighing less than 55 lbs (25 kg)) subcutaneously, intramuscularly, or intravenously. Common injection sites for GlucaGen® are upper arms, thighs, or buttocks. If the weight is not known: children younger than 6 years should be given a 0.5 mL and children 6 years and older should be given 1 mL.
- Discard any unused portion.
- Emergency assistance should be sought immediately after subcutaneous or intramuscular injection of glucagon.
- The glucagon injection may be repeated using a new kit while waiting for emergency assistance.
- Intravenous glucose MUST be administered if the patient fails to respond to glucagon.
- When the patient has responded to the treatment, give fast-acting and long-acting oral carbohydrates to restore the liver glycogen and prevent recurrence of hypoglycemia.

For GlucaGen® Diagnostic Kit and the GlucaGen® 10-pack:**2.2 Use as a diagnostic aid**

- GlucaGen® should be reconstituted with 1 mL of Sterile Water for Reconstitution (if supplied) or 1 mL of Sterile Water for Injection, USP. Using a syringe, withdraw all of the Sterile Water for Reconstitution (if supplied) or 1 mL Sterile Water for Injection, USP and inject into the GlucaGen® vial.
- Shake the vial gently until the powder is completely dissolved and no particles remain in the fluid. The reconstituted fluid should be clear and of water-like consistency.
- The reconstituted GlucaGen® gives a concentration of approximately 1 mg/mL glucagon.
- The reconstituted GlucaGen® should be used immediately after reconstitution.
- GlucaGen® must be administered by medical personnel.
- Discard any unused portion.
- Onset of action after an injection will depend on the organ under examination and route of administration [see *Pharmacodynamics* (12.2)].
- The usual diagnostic dose for relaxation of the stomach, duodenal bulb, duodenum, and small bowel is 0.2 mg to 0.5 mg given intravenously or 1 mg given intramuscularly; the usual dose to relax the colon is 0.5 mg to 0.75 mg intravenously and 1 mg to 2 mg intramuscularly [see *Pharmacodynamics* (12.2)].
- After the end of the diagnostic procedure, give oral carbohydrates to patients who have been fasting, if this is compatible with the diagnostic procedure applied.

The GlucaGen® Diagnostic Kit and the GlucaGen® 10-pack presentations are intended only for use by healthcare providers as a diagnostic aid. The GlucaGen® Diagnostic Kit and the GlucaGen® 10-pack presentations are not intended for use by patients to treat severe hypoglycemia because they are not packaged with a syringe and diluent necessary for rapid preparation and administration during an emergency outside of a healthcare facility.

3 DOSAGE FORMS AND STRENGTHS

GlucaGen® is supplied in a vial, alone, or accompanied by Sterile Water for Reconstitution (1 mL) also in a vial (10 pack or diagnostic kit). It is also supplied as GlucaGen® HypoKit®, a presentation with a disposable prefilled syringe containing 1 mL Sterile Water for Reconstitution. When the glucagon powder is reconstituted with Sterile Water for Reconstitution (if supplied) or with Sterile Water for Injection, USP, it forms a solution of 1 mg/mL (1 unit/mL) glucagon for subcutaneous, intramuscular, or intravenous injection (appearance of the powder may vary, and occasionally the powder may appear compacted).

4 CONTRAINDICATIONS

GlucaGen® is contraindicated in patients with:

- Known hypersensitivity to glucagon, lactose or any other constituent in GlucaGen®
- Pheochromocytoma [see *Warnings and Precautions* (5.1)]
- Insulinoma [see *Warnings and Precautions* (5.2)]

5 WARNINGS AND PRECAUTIONS**5.1 Pheochromocytoma**

GlucaGen is contraindicated in patients with pheochromocytoma because Glucagon may stimulate the release of catecholamines from the tumor. If the patient develops a dramatic increase in blood pressure, 5 to 10 mg of phentolamine mesylate has been shown to be effective in lowering blood pressure for the

short time that control would be needed.

5.2 Insulinoma and Glucagonoma

GlucaGen® should not be administered to patients suspected of having insulinoma. In patients with insulinoma, intravenous administration of glucagon may produce an initial increase in blood glucose; however, glucagon administration may directly or indirectly (through an initial rise in blood glucose) stimulate exaggerated insulin release from an insulinoma. A patient developing symptoms of hypoglycemia after a dose of glucagon should be given glucose orally or intravenously, whichever is most appropriate. Caution should be observed in administering GlucaGen® to patients with glucagonoma.

5.3 Hypersensitivity and Allergic Reactions

Allergic reactions may occur and include generalized rash, and in some cases anaphylactic shock with breathing difficulties, and hypotension. The anaphylactic reactions have generally occurred in association with endoscopic examination during which patients often received other agents including contrast media and local anesthetics. The patients should be given standard treatment for anaphylaxis including an injection of epinephrine if they encounter respiratory difficulties after GlucaGen® injection.

5.4 Glycogen Stores and Hypoglycemia

In order for GlucaGen® treatment to reverse hypoglycemia, adequate amounts of glucose must be stored in the liver (as glycogen). Therefore, GlucaGen® should be used with caution in patients with conditions such as prolonged fasting, starvation, adrenal insufficiency, or chronic hypoglycemia because these conditions result in low levels of releasable glucose in the liver and an inadequate reversal of hypoglycemia by GlucaGen® treatment.

5.5 Cardiac Disease

Caution should be observed when glucagon is used as an adjunct in endoscopic or radiographic procedures to inhibit gastrointestinal motility in patients with known cardiac disease.

5.6 Laboratory Tests

Blood glucose measurements may be considered to monitor the patient's response.

6 ADVERSE REACTIONS

Side effects may include nausea and vomiting at doses above 1 mg or with rapid injection. Hypotension has been reported up to 2 hours after administration in patients receiving GlucaGen® as premedication for upper GI endoscopy procedures. Glucagon exerts positive inotropic and chronotropic effects and may, therefore, cause tachycardia and hypertension. Adverse reactions indicating toxicity of GlucaGen® have not been reported. A temporary increase in both blood pressure and pulse rate may occur following the administration of glucagon. Patients taking beta-blockers might be expected to have a greater increase in both pulse and blood pressure, an increase of which will be temporary because of glucagon's short half-life [see *Drug Interactions* (7.1)]. The increase in blood pressure and pulse rate may require therapy in patients with pheochromocytoma or coronary artery disease [see *Warnings and Precautions* (5.1)]. Anaphylactic reactions may occur in some cases [see *Warnings and Precautions* (5.3)].

The following adverse reactions have been identified during postapproval use of GlucaGen®. 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.

Table 1: Frequency of Adverse Reactions

Treatment of severe hypoglycemia	
Frequency (%)	Adverse Reaction
< 10	Nausea
< 1	Vomiting
Use as a diagnostic aid	
< 10	Nausea
< 1	Vomiting
< 1	Hypoglycemia
< 1	Hypoglycemic coma

7 DRUG INTERACTIONS**7.1 Beta-blockers**

Patients taking beta-blockers might be expected to have a greater increase in both pulse and blood pressure, an increase of which will be temporary because of glucagon's short half-life. The increase in blood pressure and pulse rate may require therapy in patients with pheochromocytoma or coronary artery disease.

7.2 Indomethacin

When used with indomethacin, glucagon may lose its ability to raise blood glucose or may even produce hypoglycemia. Therefore, caution should be exercised for patients taking indomethacin when glucagon will be administered.

7.3 Anticholinergic Drugs

Coadministration with an anticholinergic drug is not recommended due to increased gastrointestinal side effects.

7.4 Warfarin

Glucagon may increase the anticoagulant effect of warfarin. Therefore, caution should be exercised for patients taking warfarin when glucagon will be administered.

7.5 Insulin

Insulin reacts antagonistically towards glucagon. Therefore, caution should be exercised when glucagon is used as a diagnostic aid in diabetes patients.

8 USE IN SPECIFIC POPULATIONS**8.1 Pregnancy**

Pregnancy Category B. Reproduction studies were performed in rats and rabbits at GlucaGen® doses of 0.4, 2.0, and 10 mg/kg. These doses represent exposures of up to 100 and 200 times the human dose based on mg/m² for rats and rabbits, respectively, and revealed no evidence of harm to the fetus. There are, however, no adequate and well-controlled studies in pregnant women. Glucagon does not cross the human placenta barrier.

8.3 Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when GlucaGen® is administered to a nursing woman. No clinical

studies have been performed in nursing mothers, however, GlucaGen® is a peptide and intact glucagon is not absorbed from the GI tract. Therefore, even if the infant ingested glucagon it would be unlikely to have any effect on the infant. Additionally, GlucaGen® has a short plasma half-life thus limiting amounts available to the child.

8.4 Pediatric Use

For the treatment of severe hypoglycemia: The use of glucagon in pediatric patients has been reported to be safe and effective.

For use as a diagnostic aid: Safety and effectiveness in pediatric patients have not been established.

10 OVERDOSAGE

No reports of overdosage with GlucaGen® have been reported. 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, the 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.

11 DESCRIPTION

GlucaGen® (glucagon [rDNA origin] for injection) is an antihypoglycemic agent and a gastrointestinal motility inhibitor. It is produced by expression of recombinant DNA in a *Saccharomyces cerevisiae* vector with subsequent purification. The chemical structure of the glucagon in GlucaGen® is identical to human glucagon and to glucagon extracted from beef and pork pancreas. Glucagon with the empirical formula of C₁₅₃H₂₂₅N₄₃O₄₉S, and a molecular weight of 3483, is a single-chain polypeptide containing 29 amino acid residues. The structure of glucagon is:



GlucaGen® is a sterile, lyophilized white powder in a 2 mL vial (appearance of the powder may vary, and occasionally the powder may appear compacted). The reconstituted solution contains glucagon as hydrochloride 1 mg/mL (1 unit/mL) and lactose monohydrate (107 mg). GlucaGen® is supplied at pH 2.5-3.5 and is soluble in water.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Antihypoglycemic Action: Glucagon induces liver glycogen breakdown, releasing glucose from the liver. Hepatic stores of glycogen are necessary for glucagon to produce an antihypoglycemic effect.

Gastrointestinal Motility Inhibition: Extra hepatic effects of glucagon include relaxation of the smooth muscle of the stomach, duodenum, small bowel, and colon.

12.2 Pharmacodynamics

For the treatment of severe hypoglycemia:

Blood glucose concentration rises within 10 minutes of injection and maximal concentrations are attained at approximately 30 minutes after injection (see Figure 1). The duration of hyperglycemic action after intravenous or intramuscular injection is 60–90 minutes.

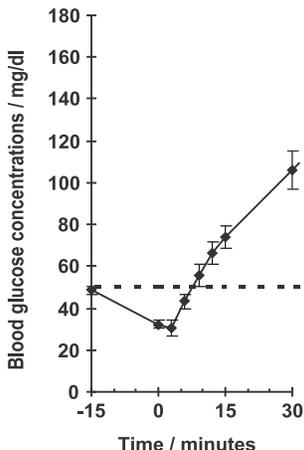


Figure 1: Recovery from Insulin Induced Hypoglycemia (mean blood glucose) After Intramuscular Injection of 1 mg GlucaGen® in Type I Diabetic Men

For use as a diagnostic aid:

Table 2: Pharmacodynamic Properties of Glucagon

Route of Administration	Dose*	Time of Maximal Glucose Concentration	Time of Onset of Action for GI Smooth Muscle Relaxation	Duration of Smooth Muscle Relaxation ¹
IV	0.25-0.5 mg (0.25-0.5 units)	5-20 minutes	45 seconds	9-17 minutes
	2 mg (2 units)	5-20 minutes	45 seconds	22-25 minutes
IM	1 mg (1 unit)	30 minutes	8-10 minutes	12-27 minutes
	2 mg (2 units)	30 minutes	4-7 minutes	21-32 minutes

*The usual diagnostic dose for relaxation of the stomach, duodenal bulb, duodenum, and small bowel is 0.2–0.5 mg given intravenously or 1 mg given intramuscularly; the usual dose to relax the colon is 0.5–0.75 mg intravenously and 1–2 mg intramuscularly.

¹Note: The time of maximal glucose concentration for GlucaGen® administered subcutaneously is 30–45 minutes.

12.3 Pharmacokinetics

Intramuscular injection of 1 mg GlucaGen® resulted in a mean C_{max} (CV%) of 1686 pg/mL (43%) and median T_{max} of 12.5 minutes. The mean apparent half-life of 45 minutes after intramuscular injection probably reflects prolonged absorption from the injection site. Glucagon is degraded in the liver, kidney, and plasma.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long term studies in animals to evaluate carcinogenic potential have not been performed. Several studies have been conducted to evaluate the mutagenic potential of glucagon. The mutagenic potential tested in the Ames and human lymphocyte assays, was borderline positive under certain conditions for both glucagon (pancreatic) and glucagon (rDNA) origin. *In vivo*, very high doses (100 and 200 mg/kg) of glucagon (both origins) gave a slightly higher incidence of micronucleus formation in male mice but there was no effect in females. The weight of evidence indicates that GlucaGen® is not different from glucagon pancreatic origin and does not pose a genotoxic risk to humans. GlucaGen® (rDNA origin) was not tested in animal fertility studies. Studies in rats have shown that pancreatic glucagon does not cause impaired fertility.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

GlucaGen® is supplied as a sterile, lyophilized white powder in a vial, alone, or accompanied by Sterile Water for Reconstitution also in a vial (Diagnostic Kit or 10-pack). It is also supplied as GlucaGen® HypoKit® with a disposable prefilled syringe containing Sterile Water for Reconstitution.

GlucaGen® HypoKit® includes:

- 1 vial containing 1 mg (1 unit) GlucaGen® (glucagon [rDNA origin] for injection)
- 1 disposable syringe containing 1 mL Sterile Water for Reconstitution
- NDC 0169-7065-15

GlucaGen® Diagnostic Kit (NDC 0597-0260-10) includes:

- 1 vial containing 1 mg (1 unit) GlucaGen® (glucagon [rDNA origin] for injection)
- NDC 0597-0053-01
- 1 vial containing 1 mL Sterile Water for Reconstitution
- NDC 0597-0265-94

GlucaGen® Diagnostic Kit is also available as NDC 55390-004-01 and includes:

- 1 vial containing 1 mg (1 unit) GlucaGen® (glucagon [rDNA origin] for injection)
- NDC 55390-004-01
- 1 vial containing 1 mL Sterile Water for Reconstitution

The GlucaGen® 10-pack includes:

- 10 vials, each containing 1 mg (1 unit) GlucaGen® (glucagon [rDNA origin] for injection)
- NDC 55390-004-10
- NDC 0597-0053-45

16.2 Recommended Storage

Before Reconstitution:

The GlucaGen® package may be stored up to 24 months at controlled room temperature 20° to 25° C (68° to 77° F) prior to reconstitution. Do not freeze. Keep in the original package to protect from light. GlucaGen® should not be used after the expiry date on the vials.

After Reconstitution:

Reconstituted GlucaGen® should be used immediately. Discard any unused portion. If the solution shows any sign of gel formation or particles, it should be discarded.

17 PATIENT COUNSELING INFORMATION

[See FDA-Approved Patient Information and Instructions for Use.]

17.1 Physician Instructions

Refer patients and family members to the FDA-approved patient labeling for instructions describing the method of preparing and injecting GlucaGen®. Advise the patient and family members to become familiar with the technique of preparing glucagon before an emergency arises. Instruct patients to use 1 mg for adults or ½ the adult dose (0.5 mg) for children weighing less than 55 lb (25 kg). To prevent severe hypoglycemia, patients and family members should be informed of the symptoms of mild hypoglycemia and how to treat it appropriately. Family members should be informed to arouse the patient as quickly as possible because prolonged hypoglycemia may result in damage to the central nervous system. Patients should be advised to inform their physician each time a hypoglycemic reaction occurs so that the treatment regimen may be adjusted if necessary.

No studies on the effects on the ability to drive and use machines have been performed. After diagnostic procedures, hypoglycemia has been reported infrequently. The patient's ability to concentrate and react may be impaired as a result of hypoglycemia. This may present a risk in situations where these abilities are especially important, such as driving or operating machinery. Therefore, these activities should be avoided until the patient has had intake of oral carbohydrates.

Date of issue: December 10, 2015

Version: 7

GlucaGen® and HypoKit® are registered trademarks of Novo Nordisk A/S

Manufactured by:
Novo Nordisk A/S
2880 Bagsvaerd, Denmark

For information contact:
Novo Nordisk Inc.
800 Scudders Mill Road
Plainsboro, New Jersey 08536
1-800-727-6500
www.novonordisk-us.com

© 1998-2016 Novo Nordisk
USA15HCP01744 1/2016



PATIENT INFORMATION
GlucaGen® (Glū-ka-Gen)
(glucagon [rDNA origin] for injection)
HypoKit®

What is GlucaGen®?

GlucaGen® is a prescription medicine used:

- to treat very low blood sugar (severe hypoglycemia) in people with diabetes who use insulin.

Who should not use GlucaGen®?

Do not use GlucaGen® if:

- you are allergic to glucagon or lactose or any of the ingredients in GlucaGen®. See the end of this Patient Information leaflet for a complete list of ingredients in GlucaGen®.
- you have a tumor in the gland on top of your kidneys (adrenal gland) called a pheochromocytoma.
- you have a tumor in your pancreas called an insulinoma.

What should I tell my doctor before using GlucaGen®?

Before using GlucaGen®, tell your doctor about all of your medical conditions, including if you:

- have kidney problems
- have pancreas problems. Tumors in your pancreas called glucagonomas.
- have not had food or water for a long time (prolonged fasting or starvation)
- have low blood sugar that does not go away (chronic hypoglycemia)
- have heart problems
- are pregnant or plan to become pregnant
- are breastfeeding or plan to breastfeed. It is not known if GlucaGen® passes into your breast milk.

Tell your doctor about all the medicines you take, including prescription and over the counter medicines, vitamins and herbal supplements. GlucaGen® may affect the way other medicines work, and other medicines may affect how GlucaGen® works. Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

How should I use GlucaGen®?

- Read the detailed **Instructions for Use** that come with GlucaGen®.
- Use GlucaGen® exactly as your doctor tells you to.
- Make sure that you and your family know how to use GlucaGen® the right way before you need it.
- Act quickly. Having low blood sugar for a period of time may be harmful.
- **Call for emergency medical help right after you use GlucaGen®.**
- Eat sugar or a sugar-sweetened product such as a regular soft drink or fruit juice as soon as you are able to swallow.
- Tell your doctor each time you use GlucaGen®. Your doctor may need to change the dose of your diabetes medicines.

What should I avoid while using GlucaGen®?

While using GlucaGen® do not:

- drive or operate machinery until you have eaten sugar or a sugar-sweetened product such as a regular soft drink or fruit juice.

What are the possible side effects of GlucaGen®?

GlucaGen® may cause serious side effects, including:

- **High blood pressure.** High blood pressure is common after taking GlucaGen® and can be severe.
- **Low blood sugar.** GlucaGen® can cause low blood sugar in patients with tumors in their pancreas called insulinomas and glucagonomas by making too much insulin in their bodies
- **Allergic reactions.** Symptoms of a serious allergic reaction to GlucaGen® may include rash, difficulty breathing, or low blood pressure (hypotension).

The most common side effects of GlucaGen® include:

- nausea
- vomiting
- temporary fast heartbeat or pounding in your chest (tachycardia).

Tell your doctor if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of GlucaGen®. For more information, ask your doctor or pharmacist. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store GlucaGen®?

- Store GlucaGen® at room temperature between 68°F to 77°F (20°C to 25°C).
- Check the expiration date on your vial of GlucaGen®. Do not use GlucaGen® if the expiration date has passed.
- Do not freeze GlucaGen®.
- Keep GlucaGen® in its original package, and keep GlucaGen® out of light.

After you mix the GlucaGen® powder and liquid:

- Use GlucaGen® right away.
- Throw away any unused GlucaGen®.
- Do not use GlucaGen® if a gel has formed, or if you see particles in the solution.

Keep GlucaGen® and all medicines out of the reach of children.

General information about the safe and effective use of GlucaGen®.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use GlucaGen® for a condition for which it was not prescribed. Do not give GlucaGen® to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about GlucaGen® that is written for health professionals.

What are the ingredients in the GlucaGen®?

Active Ingredient: glucagon [rDNA origin]

Inactive ingredients: lactose monohydrate and sterile water for reconstitution

This Patient Information has been approved by the U.S. Food and Drug Administration

Revised: December 10, 2015

GlucaGen® and HypoKit® are registered trademarks of Novo Nordisk A/S

Manufactured by: Novo Nordisk A/S, 2880 Bagsvaerd, Denmark.

For more information, go to www.novonordisk-us.com or call 1-800-727-6500.

© 1998-2016 Novo Nordisk USA15HCP01744 1/2016



Instructions for Use

**GlucaGen® (Glū-ka-Gen)
(glucagon [rDNA origin] for injection)
HypoKit®**

Read this Instructions for Use before you start using GlucaGen® and each time you get a refill. There may be new information. This information does not take the place of talking with your doctor about your medical condition or treatment. Talk to your doctor or pharmacist if you have any questions about how to use GlucaGen®.

Important:

- **Read and become familiar with this Instructions for Use before an emergency happens.**
- Show your family members and others where you keep your GlucaGen® HypoKit® and how to use it the right way.
- Call for emergency medical help right after you use GlucaGen®.
- Do not share your GlucaGen® syringes or needles with another person. You may give other people a serious infection or other people may get a serious infection from you.
- The prefilled syringe that comes with your GlucaGen® HypoKit® is meant for use with GlucaGen® only. Do not use GlucaGen® syringes to inject other medicines.

How should I store GlucaGen®?

- Store GlucaGen® at room temperature between 68°F to 77°F (20°C to 25°C).
- Check the expiration date on your vial of GlucaGen®. Do not use GlucaGen® if the expiration date has passed.
- Do not freeze GlucaGen®.
- Keep GlucaGen® in its original package, and keep GlucaGen® out of light.

After you mix the GlucaGen® powder and liquid:

- Use GlucaGen® right away.
- Throw away any unused GlucaGen®.
- Do not use GlucaGen® if a gel has formed, or if you see particles in the solution.

Supplies you will need for your GlucaGen® injection (See Figure A):

- 1 GlucaGen® HypoKit® that contains:
 - 1 vial that contains 1 mg of GlucaGen® powder (glucagon [rDNA origin] for injection) and 1 prefilled syringe with attached needle that contains 1 mL of sterile water.

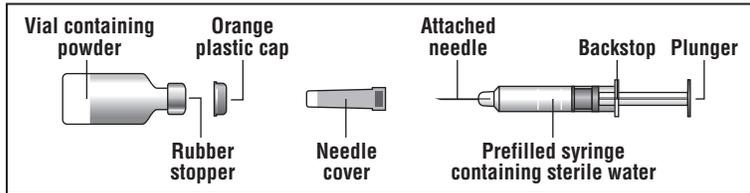


Figure A

- 1 puncture-resistant container for throwing away used needles and syringes. See "How should I dispose of (throw away) used GlucaGen® prefilled syringes" at the end of these instructions.

Preparing the GlucaGen® dose:

- The GlucaGen® medicine comes as a dry powder. Before you use GlucaGen®, you must mix the dry powder with the syringe of sterile water that comes in the GlucaGen® HypoKit®. **Do not use any other liquid to mix the medicine.**
- Check that the orange plastic cap on your vial of GlucaGen® is firmly attached. **Do not** use the vial of GlucaGen® if the orange plastic cap is loose or missing.

Step 1. Using your thumb, flip the orange plastic cap off the GlucaGen® vial (See Figure B).

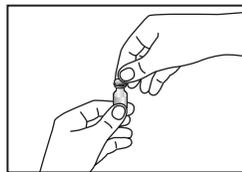


Figure B

Step 2. Pick up the prefilled syringe containing sterile water. Hold the syringe with 1 hand and with your other hand; pull the needle cover off the syringe (See Figure C).

- **Do not** remove the plastic backstop from the syringe.

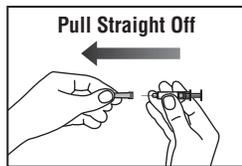


Figure C

Step 3. Pick up the GlucaGen® vial. Hold the vial of dry powder with 1 hand and with your other hand; push the needle of the prefilled syringe through the center of the rubber stopper (See Figure D).

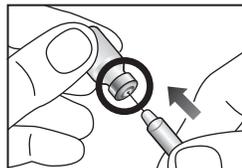


Figure D

Step 4. Hold the vial and syringe together, with the needle still inserted into the vial. Carefully turn the vial and syringe together right side up. Slowly push the plunger down until the syringe is empty (See Figure E).

- **Do not take the syringe out of the vial.**

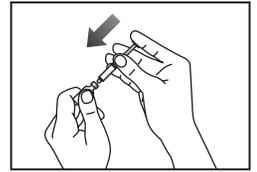


Figure E

Step 5. Hold the entire unit (the vial and syringe) in one hand and gently shake the vial until the powder is completely dissolved (See Figure F).

- Do not use if a gel has formed, or if you see particles in the solution.
- **Do not take the syringe out of the vial.**

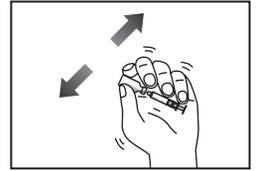


Figure F

Step 6. Firmly hold the vial and syringe together, with the needle still inserted into the vial. Carefully turn the vial and syringe together upside down. Gently pull down on the plunger and slowly withdraw all of the liquid into the syringe (See Figure G).

- Do not pull the plunger out of the syringe.

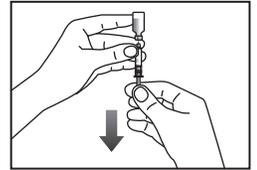


Figure G

Step 7. Keep the needle inside the vial. Check the syringe for air bubbles. If you see bubbles, tap the syringe until the bubbles rise to the top of the syringe (See Figure H). Gently push on the plunger to move only the air bubbles back into the vial.

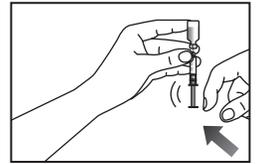


Figure H

Step 8. Hold the vial and syringe as shown (See Figure I)

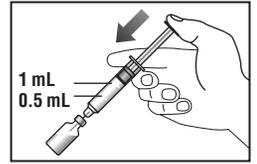


Figure I

- The usual dose for adults and children who weigh more than 55 pounds (25 kg) is 1 mg (1 mL). Use the content of the full syringe (1 mL).
- The usual dose for children who weigh less than 55 pounds (25 kg) is 0.5 mg (0.5 mL). Gently push the plunger until it is at the 0.5 mL mark on the syringe to ensure there is 0.5 mL liquid left in the syringe.

Take the syringe and needle out of the vial when the correct dose of GlucaGen® is in the syringe.

If you do not know how much the child weighs:

- Give a child under 6 years of age 0.5 mg (0.5 mL).
- Give a child 6 years of age and older 1 mg (1 mL).

Giving the GlucaGen® injection:

Step 9. Choose the injection site (See Figure J).

Common injection sites for GlucaGen® are upper arms, thighs, or buttocks.

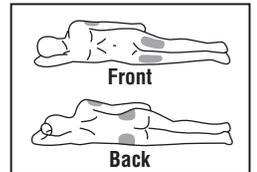


Figure J

Step 10. With one hand gently pinch the skin at the injection site. With your other hand insert the needle into the skin and push the syringe plunger down until the syringe is empty (See Figure K).

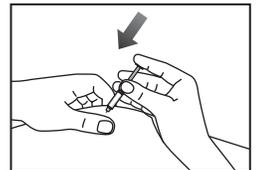


Figure K

After Giving the GlucaGen® injection:

Step 11. Pull the needle out of the skin and press on the injection site (See Figure L).

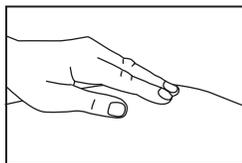


Figure L

Throw away your used syringe with the needle attached and any GlucaGen® you did not use. See **“How should I dispose of (throw away) used GlucaGen® prefilled syringes”** at the end of these instructions.

Step 12. Turn the person on their side. When an unconscious person awakens, they may vomit. Turning the person on their side will lessen the chance of choking.

Step 13. Call for emergency medical help right away.

Step 14. Feed the person as soon as they are awake and able to swallow.

Give the person a fast-acting source of sugar (such as a regular soft drink or fruit juice) and a long-acting source of sugar (such as crackers and cheese or a meat sandwich).

Step 15. Even if the GlucaGen® treatment wakes the person, tell their doctor right away. The doctor should be told whenever a severe drop in blood sugar (hypoglycemia reaction) happens. The person's dose of diabetes medicine may need to be changed.

Hypoglycemia may happen again after receiving GlucaGen® treatment.

Early symptoms of hypoglycemia may include:

- sweating
- drowsiness
- dizziness
- sleep disturbances
- irregular heartbeat (palpitation)
- anxiety
- tremor
- blurred vision
- hunger
- slurred speech
- depressed mood
- tingling in the hands, feet, lips, or tongue
- irritability
- abnormal behavior
- lightheadedness
- unsteady movement
- inability to concentrate
- personality changes
- headache
- restlessness

If not treated early, hypoglycemia may worsen and the person may have severe hypoglycemia.

Signs of severe hypoglycemia include:

- confusion
- unconsciousness
- seizures
- death

How should I dispose of (throw away) GlucaGen® pre-filled syringes?

- Put used syringes in a FDA-cleared sharps disposal container right away after use. **Do not throw away (dispose of) loose needles and syringes in your household trash.**
- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
 - made of a heavy-duty plastic,
 - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
 - upright and stable during use,
 - leak-resistant, and
 - properly labeled to warn of hazardous waste inside the container.
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: <http://www.fda.gov/safesharpsdisposal>.
- Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. Do not recycle your used sharps disposal container.

Keep GlucaGen® and all medicines out of the reach of children.

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

Revised: December 10, 2015

GlucaGen® and HypoKit® are registered trademarks of Novo Nordisk A/S

Manufactured by:
Novo Nordisk A/S
2880 Bagsvaerd, Denmark

For information contact:
Novo Nordisk Inc.
800 Scudders Mill Road
Plainsboro, NJ 08536
1-800-727-6500
www.novonordisk-us.com

© 1998-2016 Novo Nordisk
USA15HCP01744 1/2016

