

# GLUCAGEN HYPOKIT- glucagon hydrochloride

Novo Nordisk

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## 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<sup>®</sup> (glucagon) for injection, for subcutaneous, intramuscular or intravenous use**

**Initial U.S. Approval: 1998**

## ----- 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 -----

- For injection: 1 mg of glucagon as powder for reconstitution in a single dose vial, alone or co-packaged with Sterile Water for Reconstitution. (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, 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 GlucaGen is used as a diagnostic aid in diabetic patients because it may cause hyperglycemia. (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)

- Use with caution in patients with known cardiac disease, as glucagon increases myocardial oxygen demand. (5.6)

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#### ADVERSE REACTIONS

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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](http://www.fda.gov/medwatch).**

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#### DRUG INTERACTIONS

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- 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)

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#### USE IN SPECIFIC POPULATIONS

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- 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 severe 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: 11/2020**

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## **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. GlucaGen is not recommended in combination with anticholinergic agents due to the possibility of 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**

1. 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.
2. 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.
3. The reconstituted GlucaGen gives a concentration of approximately 1 mg/mL glucagon.
4. The reconstituted GlucaGen should be used immediately after reconstitution.
5. 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.

6. Discard any unused portion.
7. Emergency assistance should be sought immediately after subcutaneous or intramuscular injection of glucagon.
8. The glucagon injection may be repeated using a new kit while waiting for emergency assistance.
9. Intravenous glucose MUST be administered if the patient fails to respond to glucagon.
10. 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**

1. 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.
2. 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.
3. The reconstituted GlucaGen gives a concentration of approximately 1 mg/mL glucagon.
4. The reconstituted GlucaGen should be used immediately after reconstitution.
5. GlucaGen must be administered by medical personnel.
6. Discard any unused portion.
7. Onset of action after an injection will depend on the organ under examination and route of administration [see *Pharmacodynamics (12.2)*].
8. 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)*].
9. 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<sup>®</sup>, 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 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 GlucaGen 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, GlucaGen 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 GlucaGen 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 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.

### **5.6 Cardiac Disease**

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

### **5.7 Laboratory Tests**

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

## 6 ADVERSE REACTIONS

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

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

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. GlucaGen 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 GlucaGen. 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 GlucaGen'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.

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**

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

Necrolytic migratory erythema (NME) cases have been reported postmarketing in patients receiving continuous infusion of glucagon.

## 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**

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/m<sup>2</sup> 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) for injection is an antihypoglycemic agent and a gastrointestinal motility inhibitor for subcutaneous, intramuscular or intravenous use. 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 C<sub>153</sub>H<sub>225</sub>N<sub>43</sub>O<sub>49</sub>S, and a molecular weight of 3483, is a single-chain polypeptide containing 29 amino acid residues. The structure of glucagon is:

His-Ser-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-  
1 2 3 4 5 6 7 8 9 10 11

Lys-Tyr-Leu-Asp-Ser-Arg-Arg-Ala-Gln-Asp-Phe-  
12 13 14 15 16 17 18 19 20 21 22

Val-Gln-Trp-Leu-Met-Asn-Thr  
23 24 25 26 27 28 29

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 and lactose monohydrate (107 mg). Glucagen is supplied at pH 2.5-3.5, hydrochloric acid and/or sodium hydroxide may be added to adjust pH, 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.

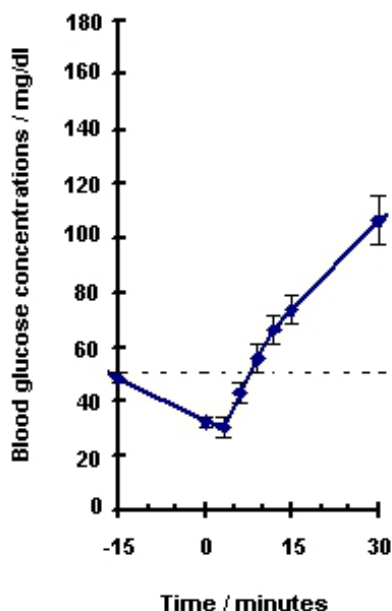


Figure 1. Recovery from Insulin Induced Hypoglycemia (mean blood glucose) after



## 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 <sup>1</sup>
IV	0.25-0.5 mg	5-20 minutes	45 seconds	9-17 minutes
	2 mg	5-20 minutes	45 seconds	22-25 minutes
IM	1 mg	30 minutes	8-10 minutes	12-27 minutes
	2 mg	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.

<sup>1</sup>Note: 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 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 (glucagon) for injection is supplied as a sterile, lyophilized white powder.

#### **GlucaGen HypoKit (NDC 0169-7065-15) includes:**

- 1 single-dose vial containing 1 mg GlucaGen (glucagon) for injection (NDC 0169-7065-15)
- 1 disposable syringe containing 1 mL Sterile Water for Reconstitution

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

- 1 single-dose vial containing 1 mg GlucaGen (glucagon) for injection (NDC 0597-0053-01)

- 1 vial containing 1 mL Sterile Water for Reconstitution (NDC 0597-0265-94)  
**GlucaGen 10-pack (NDC 0597-0053-45) includes:**
- 10 single-dose vials, each containing 1 mg GlucaGen (glucagon) for injection

## 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 GlucaGen 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.

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For information contact:

Novo Nordisk Inc.

800 Scudders Mill Road

Plainsboro, NJ 08536, USA

1-800-727-6500

www.novonordisk-us.com

Manufactured by:

Novo Nordisk A/S

2880 Bagsvaerd, Denmark

## INFORMATION FOR PATIENTS

**PATIENT INFORMATION**  
**GlucaGen® (Glū-ka-Gen)**  
**(glucagon) 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 very 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.

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**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?

### Before you mix the GlucaGen powder and liquid:

- Store GlucaGen at room temperature between 68°F to 77°F (20°C to 25°C) for up to 24 months (2 years).
- 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

**Inactive ingredients:** lactose monohydrate and sterile water for reconstitution

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

GlucaGen<sup>®</sup> and HypoKit<sup>®</sup> are registered trademarks of Novo Nordisk A/S; © 1998-2018 Novo Nordisk.

For more information, go to [www.novonordisk-us.com](http://www.novonordisk-us.com) or call 1-800-727-6500.

Revised: April 18, 2018

## **Instructions for Use**

### **GlucaGen® (Glū-ka-Gen)**

#### **(glucagon) 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?**

Before you mix the GlucaGen powder and liquid:

- 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) for injection and 1 prefilled syringe with attached needle that contains 1 mL of sterile water.

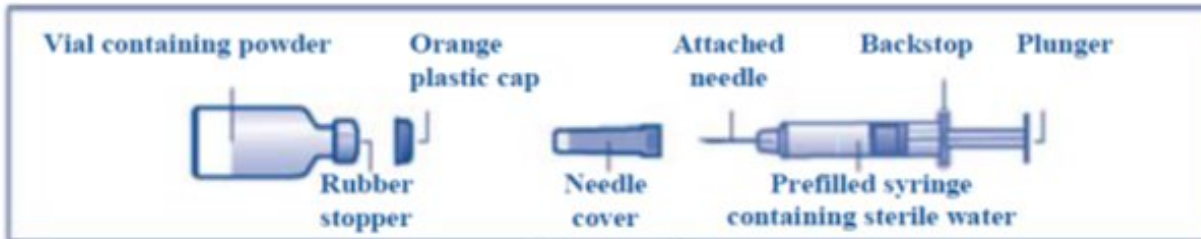


Figure A

- 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**).

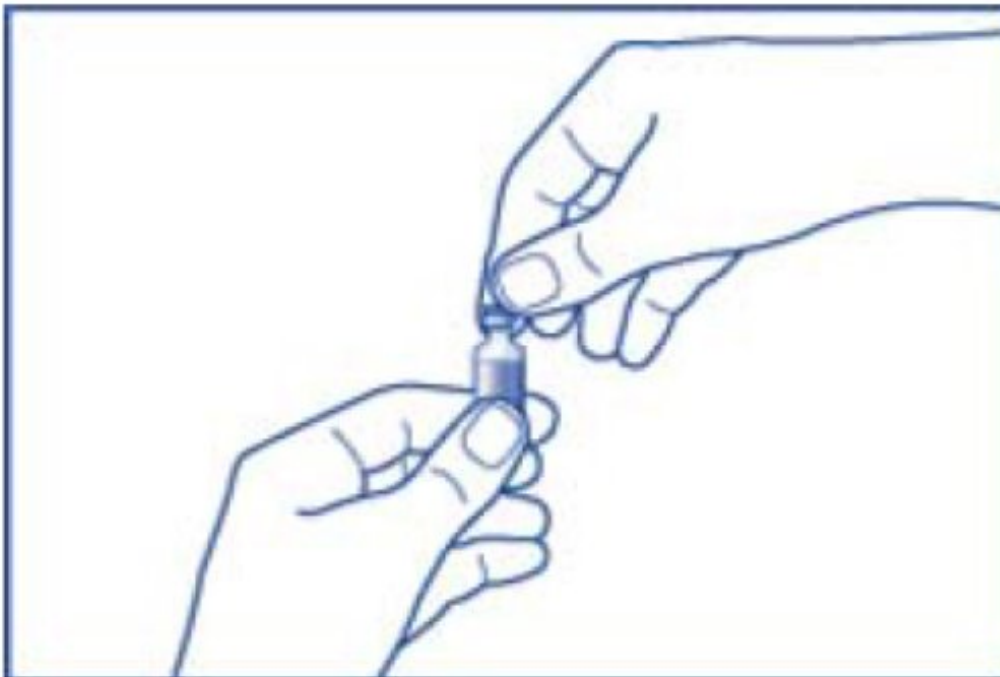


Figure B

**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.

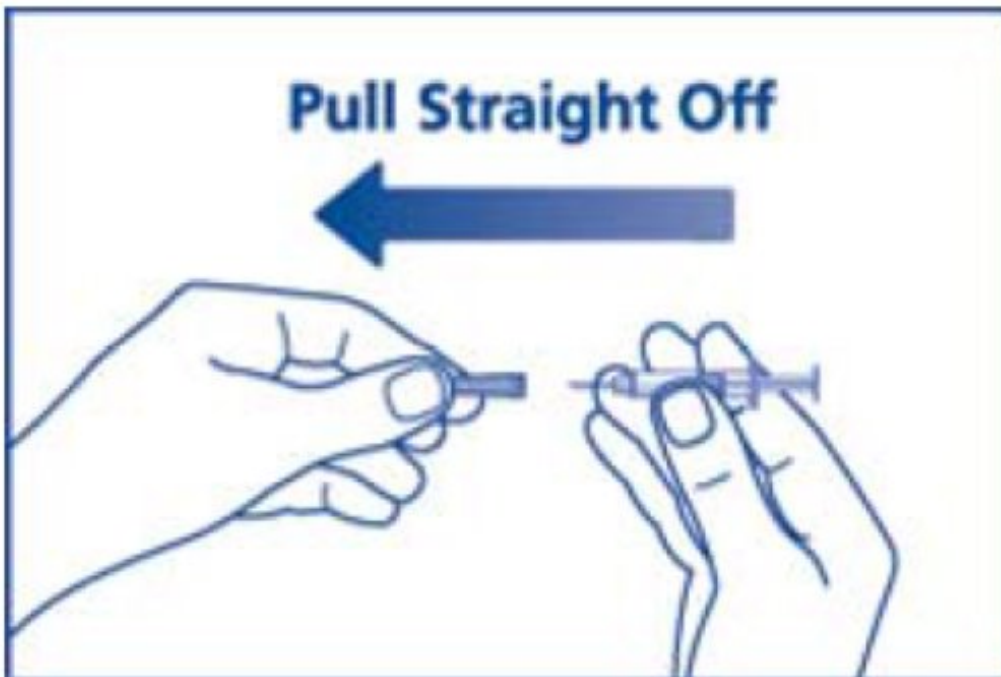


Figure C

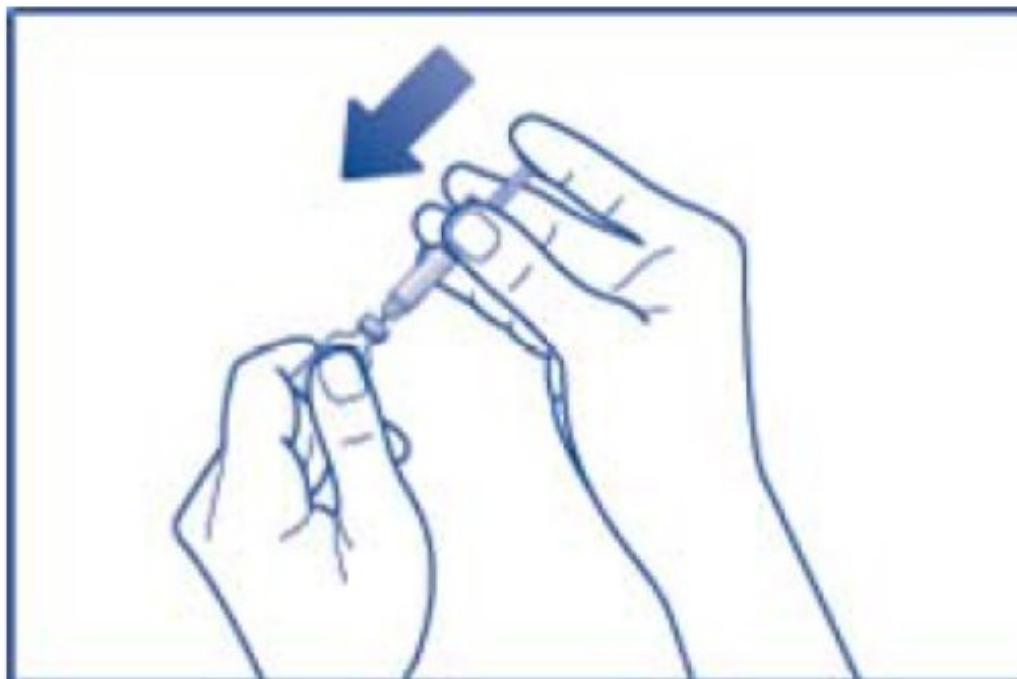
**Step 3.** Pick up the GlucaGen vial. Hold the vial of dry powder with 1 hand and with your other hand; push the needle of the prefilled syringe through the center of the rubber stopper (**See Figure D**).



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.

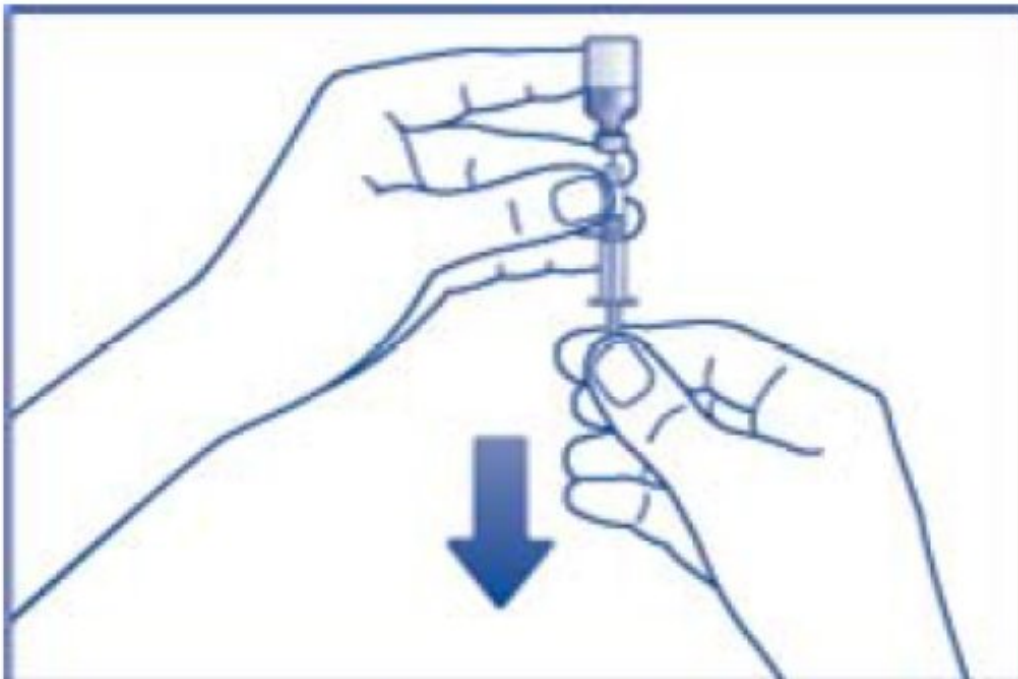


Figure G

**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.

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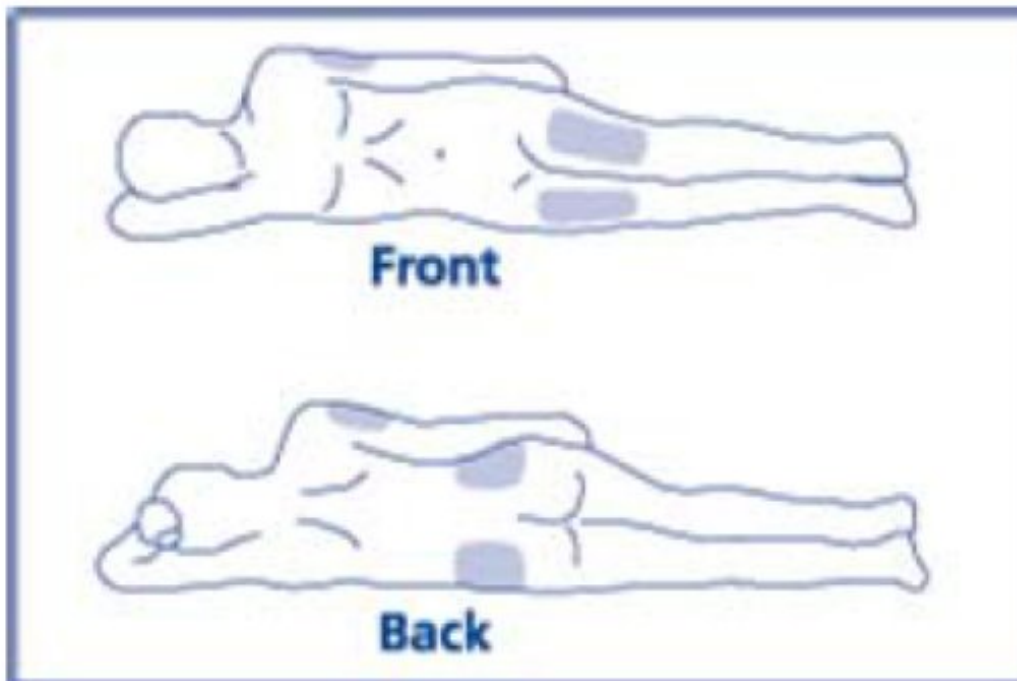
**If you do not know how much the child weighs:**

- 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**).

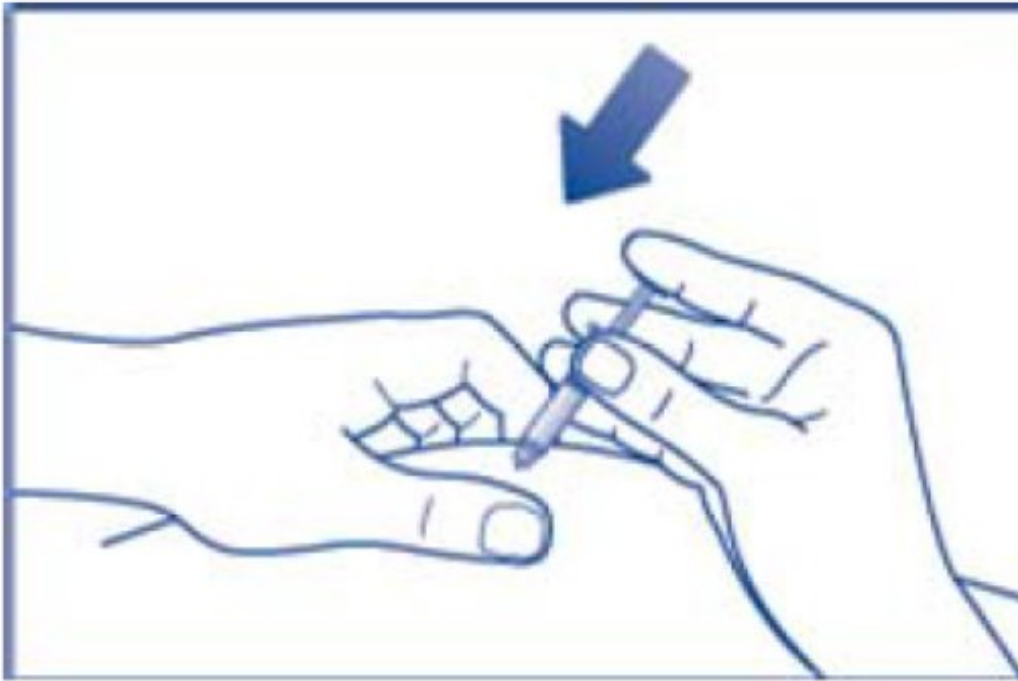


Figure K

**After Giving the GlucaGen injection:**

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

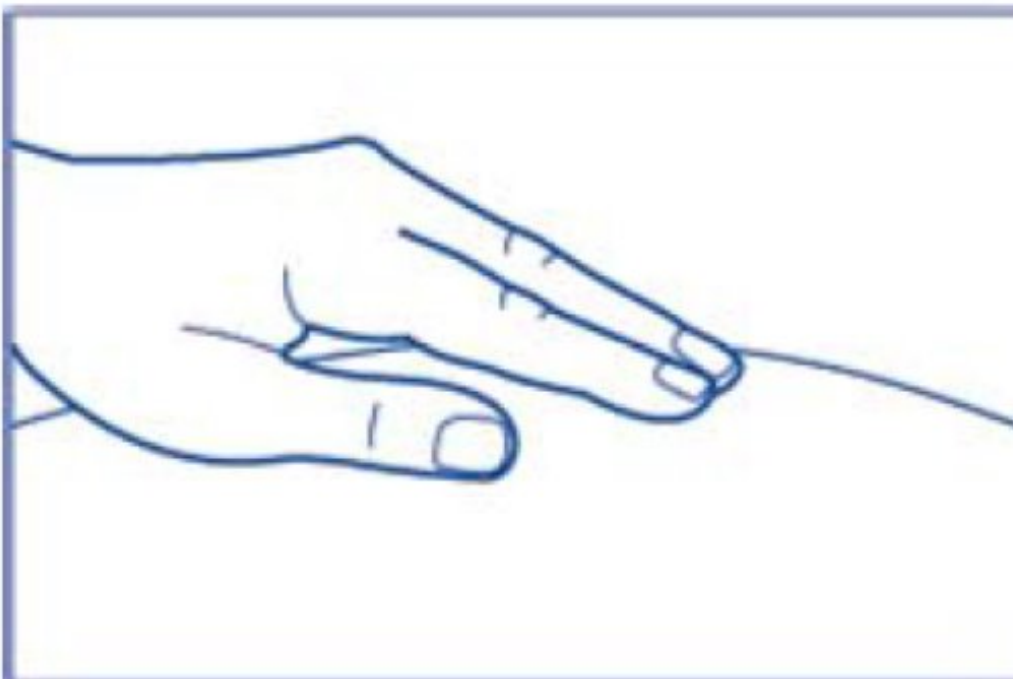


Figure L

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
  - restlessness
  - depressed mood
  - tingling in the hands, feet, lips, or tongue
  - irritability
  - abnormal behavior
  - lightheadedness
  - unsteady movement
  - inability to concentrate
  - personality changes
  - headache
- 

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.

Manufactured by:

Novo Nordisk A/S

2880 Bagsvaerd, Denmark

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For information contact:

Novo Nordisk Inc.

800 Scudders Mill Road

Plainsboro, NJ 08536

1-800-727-6500

[www.novonordisk-us.com](http://www.novonordisk-us.com)

Revised: April 18, 2018

**PRINCIPAL DISPLAY PANEL**

**NDC 0169-7065-15**

**GlucaGen® HypoKit**

(glucagon) for injection

Emergency Use for Low Blood Sugar

1 mg per vial

Single use only. Discard unused portion.

**Protect from light**

**Rx only**

Novo Nordisk Inc.

Plainsboro, NJ 08536

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1-800-727-6500

Manufactured by:

Novo Nordisk A/S

NDC 0169-7065-15  
**Glucagen® HypoKit®**  
 (glucagon) for injection  
 Emergency Use for Low Blood Sugar  
 1 mg per vial  
 Single use only. Discard unused portion.

Protect from light & use only  
 This kit contains:  
 1 vial Glucagen® for injection 1 mg,  
 1 prefilled syringe of Sterile Water for Reconstitution - for use as diluent  
 After reconstitution, the resulting Glucagen® solution contains 1 mg/mL of Glucagen.

**IMPORTANT - Read the enclosed insert carefully for directions before using.**  
**Usual Dose - 1 mg per vial for subcutaneous, intramuscular or intravenous injection in adults and pediatric patients (55 lbs or greater). Smaller pediatric patients see enclosed insert.**  
 Mix immediately before use.  
 Add the entire content of the accompanying syringe of Sterile Water for Reconstitution into the Glucagen® vial.  
 Mix well and gently withdraw the entire content of the vial back into the syringe.

**NON-RETURNABLE**  
**Before Mixing: Store at controlled room temperature 20° to 25° C (68° to 77° F)**  
 Novo Nordisk Inc.  
 Plainsboro, NJ 08536  
 www.novonordisk-us.com  
 1-800-727-6500  
 Manufactured by:  
 Novo Nordisk A/S  
 2880 Bagsvaerd, Denmark

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 ExpireLot:

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**GLUCAGEN HYPOKIT**

glucagon hydrochloride kit

**Product Information**

<b>Product Type</b>	HUMAN PRESCRIPTION DRUG	<b>Item Code (Source)</b>	NDC:0169-7065
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**Packaging**

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0169-7065-15	1 in 1 KIT; Type 0: Not a Combination Product	06/22/2005	
2	NDC:0169-7065-21	2 in 1 PACKAGE	04/25/2013	02/29/2016
2	NDC:0169-7065-15	1 in 1 KIT; Type 0: Not a Combination Product		

**Quantity of Parts**

Part #	Package Quantity	Total Product Quantity
<b>Part 1</b>	1 VIAL, GLASS	1 mL
<b>Part 2</b>	1 SYRINGE, GLASS	1 mL

**Part 1 of 2****GLUCAGEN**

glucagon hydrochloride injection, powder, for solution

**Product Information**

<b>Route of Administration</b>	INTRAMUSCULAR, INTRAVENOUS, SUBCUTANEOUS
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**Active Ingredient/Active Moiety**

Ingredient Name	Basis of Strength	Strength
GLUCAGON HYDROCHLORIDE (UNII: 1H87NVF4DB) (GLUCAGON - UNII:76LA80IG2G)	GLUCAGON	1 mg in 1 mL

**Inactive Ingredients**

Ingredient Name	Strength
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	107 mg in 1 mL

### Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1		1 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

### Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA020918	06/22/2005	

### Part 2 of 2

### WATER

water liquid

### Product Information

Route of Administration	INTRAMUSCULAR, INTRAVENOUS, SUBCUTANEOUS
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### Inactive Ingredients

Ingredient Name	Strength
WATER (UNII: 059QF0KO0R)	1 mL in 1 mL

### Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1		1 mL in 1 SYRINGE, GLASS; Type 0: Not a Combination Product		

### Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA020918	06/22/2005	

### Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA020918	06/22/2005	



## Establishment

Name	Address	ID/FEI	Business Operations
Novo Nordisk A/S		306711800	MANUFACTURE(0169-7065) , API MANUFACTURE(0169-7065)

## Establishment

Name	Address	ID/FEI	Business Operations
Catalent Belgium SA		370696762	ANALYSIS(0169-7065) , MANUFACTURE(0169-7065)

## Establishment

Name	Address	ID/FEI	Business Operations
Novo Nordisk A/S		305156788	MANUFACTURE(0169-7065)

Revised: 11/2020

Novo Nordisk