

GlucaGen®

(glucagon [rDNA origin] for injection)

Rx ONLY**DESCRIPTION**

GlucaGen® [glucagon (rDNA origin) for injection] manufactured by Novo Nordisk A/S 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 naturally occurring human glucagon and to glucagon extracted from beef and pork pancreas. Glucagon with the empirical formula of $C_{153}H_{225}N_{43}O_{49}S$, 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 11Lys-Tyr-Leu-Asp-Ser-Arg-Arg-Ala-Gln-Asp-Phe-
12 13 14 15 16 17 18 19 20 21 22Val-Gln-Trp-Leu-Met-Asn-Thr
23 24 25 26 27 28 29

GlucaGen® 1 mg (1 IU) is supplied as a sterile, lyophilized white powder in a 2 ml vial, alone, or accompanied by Sterile Water for Reconstitution (1 ml) also in a 2 ml vial (10 pack or diagnostic kit). It is also supplied as a HypoKit with a disposable prefilled syringe containing 1 ml Sterile Water for Reconstitution. Glucagon, as supplied at pH 2.5-3.5, is soluble in water.

Active Ingredient in each vial

Glucagon as hydrochloride 1 mg (corresponding to 1 IU).

Other Ingredients

Lactose monohydrate (107 mg)

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 (1 IU)/ml glucagon for subcutaneous (sc), intramuscular (im), or intravenous (iv) injection.

GlucaGen® is an antihypoglycemic agent, and a gastrointestinal motility inhibitor.

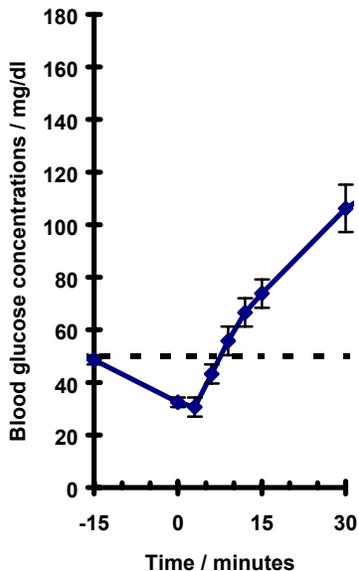
CLINICAL PHARMACOLOGY

Intramuscular (im) injection of 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 im injection probably reflects prolonged absorption from the injection site. Glucagon is degraded in the liver, kidney, and plasma.

Antihypoglycemic Action:

Glucagon induces liver glycogen breakdown, releasing glucose from the liver. Blood glucose concentration rises within 10 minutes of injection and maximal concentrations are attained at approximately a half hour after injection (see Figure). Hepatic stores of glycogen are necessary for glucagon to produce an antihypoglycemic effect.

50 Recovery from insulin induced hypoglycemia (mean blood glucose) after im injection of 1 mg GlucaGen® in Type I
51 diabetic men



52
53 **Gastrointestinal Motility Inhibition:** Extra hepatic effects of glucagon include relaxation of the smooth
54 muscle of the stomach, duodenum, small bowel, and colon.

56 INDICATIONS AND USAGE

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

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64 *For use as a diagnostic aid:*
65 GlucaGen® is indicated for use during radiologic examinations to temporarily inhibit movement of the
66 gastrointestinal tract. Glucagon is as effective for this examination as are the anticholinergic drugs.
67 However, the addition of the anticholinergic agent may result in increased side effects. Because
68 GlucaGen® depletes glycogen stores, the patient should be given oral carbohydrates as soon as the
69 procedure is completed.

71 CONTRAINDICATIONS

72 Glucagon is contraindicated in patients with known hypersensitivity to glucagon or any constituent in
73 GlucaGen® and in patients with pheochromocytoma or with insulinoma.

74 WARNINGS

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76 GlucaGen® should be administered cautiously to patients suspected of having pheochromocytoma or
77 insulinoma. Secondary hypoglycemia may occur and should be countered by adequate carbohydrate
78 intake following glucagon treatment.
79 Glucagon may release catecholamines from pheochromocytomas and is contraindicated in patients with
80 this condition.

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

87 PRECAUTIONS

88 General

89 In order for GlucaGen[®] treatment to reverse hypoglycemia, adequate amounts of glucose must be stored
90 in the liver (as glycogen). Therefore, GlucaGen[®] should be used with caution in patients with conditions
91 such as prolonged fasting, starvation, adrenal insufficiency or chronic hypoglycemia because these
92 conditions result in low levels of releasable glucose in the liver and an inadequate reversal of
93 hypoglycemia by GlucaGen[®] treatment. Caution should be observed when glucagon is used in diabetic
94 patients or in elderly patients with known cardiac disease to inhibit gastrointestinal motility.

96 Information for Patients

97 Refer patients and family members to the “INFORMATION FOR PATIENTS” for instructions
98 describing the method of preparing and injecting GlucaGen[®]. Advise the patient and family members to
99 become familiar with the technique of preparing glucagon before an emergency arises. Instruct patients
100 to use 1 mg for adults or ½ the adult dose (0.5 mg) for children weighing less than 55 lb (25 kg). To
101 prevent severe hypoglycemia, patients and family members should be informed of the symptoms of mild
102 hypoglycemia and how to treat it appropriately. Family members should be informed to arouse the
103 patient as quickly as possible because prolonged hypoglycemia may result in damage to the central
104 nervous system. Patients should be advised to inform their physician when hypoglycemic reactions
105 occur so that the treatment regimen may be adjusted if necessary.

107 Laboratory Tests

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

110 Carcinogenesis, Mutagenesis, Impairment of Fertility

111 Long term studies in animals to evaluate carcinogenic potential have not been performed. Several
112 studies have been conducted to evaluate the mutagenic potential of glucagon. The mutagenic potential
113 tested in the Ames and human lymphocyte assays, was borderline positive under certain conditions for
114 both glucagon (pancreatic) and glucagon (rDNA) origin. *In vivo*, very high doses (100 and 200 mg/kg)
115 of glucagon (both origins) gave a slightly higher incidence of micronucleus formation in male mice but
116 there was no effect in females. The weight of evidence indicates that GlucaGen[®] is not different from
117 glucagon pancreatic origin and does not pose a genotoxic risk to humans.
118 GlucaGen[®] was not tested in animal fertility studies. Studies in rats have shown that pancreatic
119 glucagon does not cause impaired fertility.¹

121 Pregnancy-Pregnancy Category B

122 Reproduction studies were performed in rats and rabbits at GlucaGen[®] doses of 0.4, 2.0, and 10 mg/kg.
123 These doses represent exposures of up to 100 and 200 times the human dose based on mg/m² for rats
124 and rabbits, respectively, and revealed no evidence of harm to the fetus. There are, however, no
125 adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not
126 always predictive of human response, this drug should be used during pregnancy only if clearly needed.

128 Nursing Mothers

129 It is not known whether this drug is excreted in human milk. Because many drugs are excreted in
130 human milk, caution should be exercised when GlucaGen[®] is administered to a nursing woman.
131 No clinical studies have been performed in nursing mothers, however, GlucaGen[®] is a peptide and intact
132 glucagon is not absorbed from the GI tract. Therefore, even if the infant ingested glucagon it would be
133 unlikely to have any effect on the infant. Additionally, GlucaGen[®] has a short plasma half-life thus
134 limiting amounts available to the child.

135
136 **Pediatric Use** For the treatment of hypoglycemia: The use of glucagon in pediatric patients has been
137 reported to be safe and effective.^{2,3,4,5}

138 For use as a diagnostic aid: Safety and effectiveness in pediatric patients have not been established.
139

140 **ADVERSE REACTIONS**

141 Severe side effects are very rare, although nausea and vomiting may occur occasionally especially with
142 doses above 1 mg or with rapid injection (less than 1 minute).¹ Hypotension has been reported up to 2
143 hours after administration in patients receiving GlucaGen[®] as premedication for upper GI endoscopy
144 procedures. Glucagon exerts positive inotropic and chronotropic effect and may, therefore, cause
145 tachycardia and hypertension. Adverse reactions indicating toxicity of GlucaGen[®] have not been
146 reported. A transient increase in both blood pressure and pulse rate may occur following the
147 administration of glucagon. Patients taking β -blockers might be expected to have a greater increase in
148 both pulse and blood pressure, an increase of which will be transient because of glucagon's short half-
149 life. The increase in blood pressure and pulse rate may require therapy in patients with
150 pheochromocytoma or coronary artery disease. (see OVERDOSAGE).
151 Allergic reactions may occur in rare cases. (see WARNINGS).
152

153 **OVERDOSAGE**

154 **Signs and Symptoms**

155 No reports of overdosage with GlucaGen[®] have been reported. It is expected, if overdosage occurred,
156 that the patient may experience nausea, vomiting, inhibition of GI tract motility, increase in blood
157 pressure and pulse rate.¹ In case of suspected overdosing, the serum potassium may decrease and should
158 be monitored and corrected if needed.

159 The IV and SC LD₅₀ for GlucaGen[®] in rats and mice ranges from 100 to greater than 200 mg/kg body
160 weight.

161 **Treatment**

162 Standard symptomatic treatment may be undertaken if overdosage occurs. If the patient develops a
163 dramatic increase in blood pressure, 5 to 10 mg of phentolamine mesylate has been shown to be
164 effective in lowering blood pressure for the short time that control would be needed. It is unknown
165 whether GlucaGen[®] is dialyzable, but such a procedure is unlikely to provide any benefit given the short
166 half-life and nature of the symptoms of overdose.
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DOSAGE AND ADMINISTRATION

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Directions for 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. Roll the vial gently until 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. Discard any unused portion. Inject 1 ml (adults and children, weighing more than 55 lbs) or ½ ml (children weighing less than 55 lbs) subcutaneously (s.c), intramuscularly (i.m), or intravenously (i.v). If the weight is not known: Children younger than 6 to 8 years should be given half dose (=½ ml) and children older than 6 to 8 should be given the adult dose (1ml).^{1,2,3,4,5,6} Emergency assistance should be sought if the patient fails to respond within 15 minutes after subcutaneous or intramuscular injection of glucagon. The glucagon injection may be repeated while waiting for emergency assistance.¹ Intravenous glucose MUST be administered if the patient fails to respond to glucagon. When the patient has responded to the treatment, give oral carbohydrate to restore the liver glycogen and prevent recurrence of hypoglycemia.

Directions for use as a diagnostic aid:

GlucaGen® should be reconstituted with the supplied 1 ml of Sterile Water for Reconstitution (if supplied) or 1 ml 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. Roll the vial gently until 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. Discard any unused portion. When the diagnostic procedure is over, give oral carbohydrate to restore the liver glycogen and prevent occurrence of secondary hypoglycemia.

References for diagnostic aid use only:

Time of maximal glucose concentration

Intravenous: 5 to 20 minutes
Intramuscular: 30 minutes
Subcutaneous: 30 to 45 minutes

Time for GI smooth muscle relaxation¹

Intravenous: 0.25 to 2 mg (IU) - 45 seconds
Intramuscular:
1 mg (IU) - 8 to 10 minutes
2 mg (IU) - 4 to 7 minutes

Duration of action -

Hyperglycemic action - 60 to 90 minutes
Smooth muscle relaxation -¹
Intravenous:
0.25 to 0.5 mg (IU) - 9 to 17 minutes
2 mg (IU) - 22 to 25 minutes
Intramuscular:
1 mg (IU) - 12 to 27 minutes
2 mg (IU) - 21 to 32 minutes

STABILITY AND STORAGE

Before Reconstitution:

215 The GlucaGen[®] package may be stored up to 24 months at controlled room temperature 20° to 25° C
216 (68° to 77° F) prior to reconstitution. Avoid freezing and protect from light. GlucaGen[®] should not be
217 used after the expiry date on the vials.

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219 **After Reconstitution:**
220 Reconstituted GlucaGen[®] should be used immediately. Discard any unused portion. If the solution
221 shows any sign of gel formation or particles, it should be discarded.

222 **HOW SUPPLIED**

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224 **GlucaGen[®] HypoKit includes:**
225 1 vial containing 1 mg (1 IU) GlucaGen[®] [glucagon (rDNA origin) for injection]
226 1 disposable syringe containing 1 ml Sterile Water for Reconstitution
227 NDC 55390-004-xx

228 OR

229 **GlucaGen[®] Diagnostic Kit includes:**
230 1 vial containing 1 mg (1 IU) GlucaGen[®] [glucagon (rDNA origin) for injection]
231 1 vial containing 1ml Sterile Water for Reconstitution
232 NDC 55390-004-01

233 OR

234 **The GlucaGen[®] 10-pack includes:**
235 10x1 vial containing 1 mg (1 IU) GlucaGen[®] [glucagon (rDNA origin) for injection]
236 NDC 55390-004-10

237
238 Edition: December 2004
239

240 **REFERENCES:**

- 241 1. *Drug Information for the Health Care Professional*. 17th ed. Rockville, Maryland: The United States
242 Pharmacopeial Convention, Inc; 1997; Vol. 1, IA: 1516-1518.
- 243 2. Gibbs et al: Use of Glucagon to terminate insulin reactions in diabetic children. *Nebr Med J*
244 1958;43:56-57.
- 245 3. Carson MJ, Koch R, Clinical studies with glucagon in children. *J Pediatr* 1955; 47:161-170.
- 246 4. Shipp JC, et al: Treatment of insulin hypoglycemia in diabetic campers. *Diabetes* 1964; 13:645-648.
- 247 5. Aman J, Wranne L: Hypoglycemia in childhood diabetes II: Effect of subcutaneous or intramuscular
248 injection of different doses of glucagon. *Acta Pediatr Scand* 1988; 77:548-553.
- 249 6. Aynsley-Green AS, Eyre JA, and Soltesz G, Hypoglycaemia in diabetic children. In: Frier BM and
250 Fisher BM, eds *Hypoglycaemia and Diabetes*, Edward Arnold, 1993; 237-238.

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252 8-9402-31-001-1

INFORMATION FOR PATIENTS

GlucaGen® HypoKit
Emergency Use for Low Blood Sugar
(glucagon [rDNA origin] for injection) 1 mg.

BECOME FAMILIAR WITH THE FOLLOWING INSTRUCTIONS BEFORE AN EMERGENCY ARISES. DO NOT USE THIS PACKAGE AFTER THE EXPIRATION DATE. IF YOU HAVE QUESTIONS CONCERNING THE USE OF THIS PRODUCT, CONSULT A DOCTOR, NURSE, OR PHARMACIST.

Make sure that your relatives or close friends know that if you become unconscious, medical assistance must always be sought. GlucaGen® may have been prescribed so that members of your household can give the injection if you become hypoglycemic (low blood sugar) and are unable to take sugar by mouth. If you are unconscious, GlucaGen® can be given while awaiting medical assistance.

Show your family members and others where you keep this kit and how to use it. They need to know how to prepare it before you need it. They can practice giving a shot by giving you your normal insulin shots. It is important that they practice. A person who has never given a shot probably will not be able to do it in an emergency.

IMPORTANT

- Act quickly. Prolonged unconsciousness may be harmful.
- These simple instructions will help you give glucagon successfully.
- Turn patient on his/her side to prevent choking.
- The content of the syringe does not contain glucagon. You must mix the contents of the syringe with the glucagon in the accompanying bottle before giving injection. (see DIRECTIONS FOR USE)
- Do not mix GlucaGen® until you are ready to use it.
- Discard any unused portion.
- Become familiar with the technique of preparing glucagon before an emergency arises.
- **WARNING: THE PATIENT MAY BE IN A COMA FROM SEVERE HYPERGLYCEMIA (HIGH BLOOD SUGAR) RATHER THAN HYPOGLYCEMIA (LOW BLOOD SUGAR). IN SUCH A CASE, THE PATIENT WILL NOT RESPOND**

TO GLUCAGON AND REQUIRES IMMEDIATE MEDICAL ATTENTION.

INDICATION FOR USE

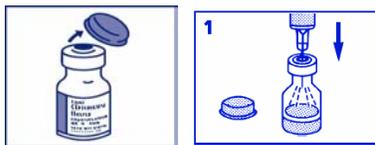
GlucaGen[®] is used to treat severe hypoglycemic (low blood sugar) reactions which may occasionally occur in patients with diabetes. Symptoms of severe hypoglycemic reactions include disorientation, loss of consciousness, and seizures. You should only give GlucaGen[®] injection if (1) the patient is unconscious, (2) the patient is having a seizure, or (3) the patient is disoriented and unable to eat sugar or a sugar-sweetened product. Milder cases of hypoglycemia should be treated promptly by eating sugar or a sugar sweetened product such as a regular soft drink or fruit juice. GlucaGen does not work if it is taken by mouth.

DIRECTIONS FOR USE:

To Prepare GlucaGen[®] For Injection:

Use the enclosed prefilled disposable syringe with the attached needle to reconstitute GlucaGen[®] before giving the injection.

Step 1. Take off the orange plastic cap off the vial. Pull the needle cover off the syringe. Insert the needle through the rubber stopper of the vial containing GlucaGen[®] and inject all the liquid from the syringe into the vial.



Step 1

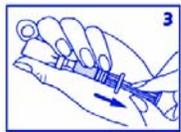
Step 2. Without taking the syringe with a needle out of the vial, gently shake the vial in your hand until the powder has completely dissolved, and the solution is clear.



Step 2

Step 3. While the needle is still inside the vial, turn the vial upside down and while keeping the needle in the liquid, slowly withdraw all the liquid into the syringe. **Be careful not to pull the plunger out of the syringe.** This will also help minimize the leakage of the fluid around the syringe. The usual dose for adult and children weighing more than 55 lbs is 1 mg (1 ml). Therefore, withdraw the solution to 1 ml mark on the syringe. The usual dose for

children weighing less than 55 lb is 0.5 mg (1/2 adult dose). Therefore, withdraw 1/2 of the solution from the vial (0.5 ml mark on the syringe) for these children. DISCARD UNUSED PORTION.



Step 3

To Inject GlucaGen®

Step 4. Turn the patient on his/her side. When an unconscious person awakens, he/she may vomit. Turning the patient on his/her side will prevent him/her from choking. Without removing the needle from the vial and while keeping the needle in the liquid, remove any air bubble(s) in the syringe by flicking the syringe with your finger and squirting any air bubbles out of the needle into the vial. Continue pushing the plunger until you have the correct dose as described in Step 3. In the event the plunger is pushed below the required dose, pull back the plunger until you have the correct dose. When you have a correct amount of glucagon in the syringe, pull the syringe with a needle from the vial. Insert the needle into the loose tissue under the injection site, and inject the glucagon solution. THERE IS NO DANGER OF OVERDOSE.



Step 4

After Giving the Injection

Step 5. Withdraw the needle and press on the injection site. Used syringe and needle should be placed in sharps containers (such as red biohazard containers), hard plastic containers (such as detergent bottles), or metal containers (such as an empty coffee can). Such containers should be sealed and disposed of properly.

Step 6. FEED THE PATIENT AS SOON AS HE/SHE AWAKENS AND IS ABLE TO SWALLOW. Give the patient 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). If the patient does not awaken within 15 minutes, give another dose of GlucaGen

and INFORM A DOCTOR OR EMERGENCY SERVICES IMMEDIATELY.

Step 7. Even if the GlucaGen awakens the patient, his/her doctor should be promptly notified. A doctor should be notified whenever severe hypoglycemic reactions happen.

How GlucaGen® Works

GlucaGen® (glucagon [rDNA origin] for injection) is quickly absorbed after injection under the skin or into the muscle. Glucagon action causes glucose (sugar) to be released from the liver where it is stored as glycogen. Blood sugar levels increase within 10 minutes of injection and reach the highest amount approximately half an hour after injection. Glucagon works by promoting the release of glycogen (stored sugar in the liver).

When GlucaGen® Should Not Be Used

Do not use GlucaGen® if a patient is allergic to glucagon.

WARNINGS

Hypoglycemia may occur again following glucagon treatment. Tell your friends or relatives that you must be given a fast-acting source of sugar (such as regular soft drink or fruit juice), followed by a long acting source of sugar (carbohydrates) by mouth as soon as you are able to take it after you have responded to treatment - this will prevent the return of hypoglycemia (low blood sugar). Early symptoms of hypoglycemia may include:

- perspiration
- drowsiness
- dizziness
- sleep disturbances
- 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

Allergic reactions may occur rarely and include generalized rash, anaphylactic shock, breathing difficulties and hypotension (low blood pressure).

Keep **this kit** out of reach of children.

PRECAUTIONS

General - GlucaGen[®] is only of benefit in hypoglycemia (low blood sugar) when the liver has sufficient glucose (in the form of glycogen) to release. For that reason GlucaGen[®] has little or no effect if you are fasting, or if you are suffering from adrenal insufficiency, chronic hypoglycemia or alcohol induced hypoglycemia. Remember GlucaGen[®] has the opposite effect of insulin.

If the GlucaGen solution shows any sign of gel formation or particles it should be discarded.

Your GlucaGen[®] HypoKit for hypoglycemia (low blood sugar) includes:

- One vial of 1 mg GlucaGen[®] (glucagon [rDNA origin] for injection)
- One prefilled disposable syringe with attached needle containing 1 ml Sterile Water for Reconstitution

The vial has a protective plastic cap. You must remove the plastic cap to inject the water and reconstitute the freeze-dried GlucaGen[®]. If the cap is loose or missing when you buy the package, return it to your local pharmacy.

Pregnancy - GlucaGen[®] is glucagon which is a hormone that is always present in humans. GlucaGen[®] is intended for infrequent use during acute, severe hypoglycemic attacks, and may be used during pregnancy.

Nursing Mothers - Breast feeding following treatment with GlucaGen[®] for your hypoglycemic attack should not put your baby at risk. GlucaGen[®] does not stay very long in the body. Also, because glucagon is a protein, even if the infant ingested glucagon, it would be unlikely to have any effect on the infant because it would be digested.

POSSIBLE PROBLEMS WITH GlucaGen[®] TREATMENT

Severe side effects are very rare, although nausea and vomiting may occur occasionally. Side effects indicating toxicity of GlucaGen[®] have not been reported.

A few people may be allergic to glucagon or to one of the inactive ingredients in GlucaGen[®], or may experience rapid heart beat for a short while.

If you experience any other reactions which are likely to have been caused by GlucaGen[®], please contact your doctor.

EXPIRATION DATE

Before mixing - 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. Avoid freezing and protect from light. Never use GlucaGen[®] after the expiration date printed on the package.

GlucaGen® does not contain preservatives and is for single use only.

After mixing - Reconstituted GlucaGen® should be used immediately. Discard any unused portion.

Date of Printing: mmyyyy (Revision #x)
Circular #

GlucaGen® is a registered trademark of Novo Nordisk A/S

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

For information contact:
Novo Nordisk Inc.
Princeton, New Jersey 08540
1-800-727-6500
www.novonordisk-us.com

8-9402-31-001-1

First display Panel:

<p style="text-align: center;">NDC xxxx-xxxx-xx</p> <p style="text-align: center;">GlucaGen® HypoKit Emergency Use for Low Blood Sugar</p> <p style="text-align: center;">(glucagon [rDNA origin] for injection) 1 mg (1 unit)</p>
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Second display panel:

<p>Rx only</p> <p>This kit contains: 1 vial GlucaGen® for injection 1 mg, 1 prefilled syringe of Sterile Water for Reconstitution – for use as diluent</p> <p>Once GlucaGen® is reconstituted with the prefilled syringe of Sterile Water for Reconstitution, the resulting solution contains 1 mg/mL of glucagon</p> <p>IMPORTANT – Read the enclosed insert carefully for directions before using.</p>

Third display panel

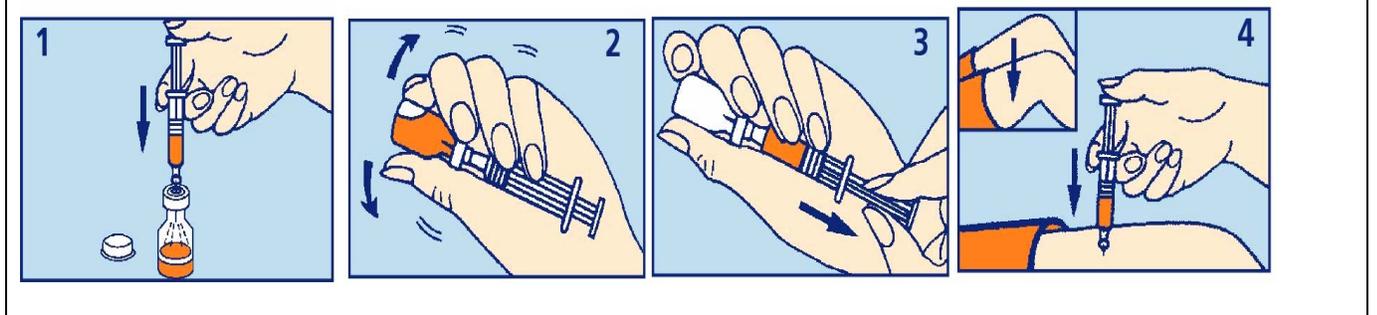
<p>Usual Dose - 1 mg (1 unit) sc, im, or iv adults and pediatric patients (55 lbs or greater). Smaller pediatric patients see enclosed insert.</p> <p>Mix immediately before use by adding the entire contents of the accompanying syringe containing Sterile Water for Reconstitution into the vial containing GlucaGen® powder. Mix well and gently withdraw the entire contents of the vial back into the syringe. Solution should be clear and of a water-like consistency at time of use.</p>

Fourth display panel:

<p>Before Mixing: Store at controlled room temperature 20° to 25° C (68° to 77° F) After Mixing: Should be used immediately</p> <p>DISCARD ANY UNUSED PORTION.</p> <p>PHARMACIST: Please detach 'INFORMATION FOR PATIENTS' and give to the patient</p> <p>Novo Nordisk, Inc. Princeton, NJ 08540 www.novonordisk-us.com 1-800-727-6500</p> <p>Manufactured by: Novo Nordisk A/S 2880 Bagsvaerd, Denmark</p> <p><i>(Bar Code)</i> <i>(Exp. Date)</i> <i>(Lot No.)</i></p>

(8-xxxx-xx-xxx-x)

Inside Lid:



Container Label (GlucaGen® Vial)

<p>GlucaGen® (glucagon [rDNA origin] for injection) 1 mg</p> <p>Glucagon as Hydrochloride 1mg (1 unit) For s.c., i.m., or i.v. injection</p>	<p>NDC xxxx-xxx-xx Rx ONLY Must be diluted with enclosed diluent (Sterile Water for Reconstitution) prior to use</p> <p>Novo Nordisk, Inc.</p>	<p>RSS Code 8-9400-31-203-1 EXP/Lot:</p>
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NDA 20-918

Page 1

Container Label (Sterile Water for Reconstitution syringe):

1 ml
Sterile Water for Reconstitution
Drug Diluent Use Only

Novo Nordisk, Inc.

Exp:

Lot: