PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

1 NAME OF THE MEDICINE

GlucaGen Hypokit Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

A vial containing bio-synthetic glucagon as hydrochloride as a freeze dried powder equivalent to glucagon 1 mg.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder and solvent for solution for injection.

A sealed vial with a white or nearly white compacted powder.

Water for Injections: clear and colourless solution, without particles, in a syringe.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

- GlucaGen Hypokit is indicated for treatment of severe hypoglycaemic reactions, which may occur in the management of insulin treated children and adults with diabetes mellitus.

- GlucaGen Hypokit is indicated for motility inhibition in examinations of the gastrointestinal tract in adults.

4.2 Posology and method of administration

In the absence of oral/IV dextrose, GlucaGen Hypokit is administered subcutaneously or intramuscularly for the treatment of hypoglycaemia. On regaining consciousness, the patient should be given food rich in carbohydrate to restore the liver glycogen and prevent secondary hypoglycaemia. If the patient does not respond within 10 minutes, intravenous glucose should be given.

GlucaGen Hypokit should be used immediately after preparation.

There are no known incompatibilities with GlucaGen Hypokit.

Severe hypoglycaemia:

Dosage for adult patients: Administer 1 mg.

Special populations

Paediatric population (< 18 years old):

GlucaGen Hypokit can be used for the treatment of severe hypoglycaemia in children and adolescents.

Dosage for paediatric patients: Administer 1 mg (children above 25 kg or older than 6 - 8 years) or 0,5 mg (children below 25 kg or younger than 6 - 8 years).

Elderly (≥ 65 years old):

GlucaGen Hypokit can be used in elderly patients.

Renal and hepatic impairment:

GlucaGen Hypokit can be used in patients with renal and hepatic impairment.

Method of administration

GlucaGen Hypokit Administration Guide

Snap-off Caps

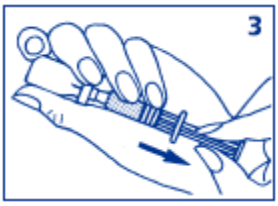
The GlucaGen Hypokit vials are packed with a protective tamper-proof plastic cap. In order to inject Water for Injections into the vial with GlucaGen Hypokit, the cap must be removed. Do not use the injection if the cap is not securely fastened.



1. Pull the needle cover off the syringe. Do not remove the plastic back-stop from the syringe. Insert the needle through the rubber stopper (within the marked circle) of the vial. Inject the Water for Injections into vial containing freeze-dried GlucaGen Hypokit.



2. Without withdrawing the syringe, shake the vial until the contents are completely dissolved, and the solution is clear.

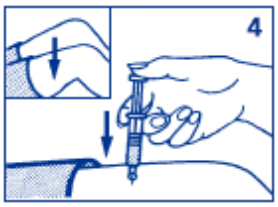


3. Make sure the plunger is completely down. While keeping the needle in the liquid, slowly withdraw all the solution back into the syringe. Do not pull the plunger out of the syringe. It is important to remove any air bubbles from the syringe:

• With the needle pointing upwards, tap the syringe with your finger;

• Push the plunger slightly to release any air that has collected at the top of the syringe.

Continue to push the plunger until you have the correct dose for injection. A small amount of liquid will be pushed out when you do this.



4. Inject the dose under the skin or into a muscle.

5. Turn the unconscious person on their side to prevent choking.

6. Give the person a high sugar snack like sweets, biscuits or fruit juice as soon as he or she regains consciousness and is able to swallow. This is because GlucaGen Hypokit. empties glycogen stores. The high sugar snack will prevent relapse of the hypoglycaemia.

Inhibition of gastrointestinal motility:

GlucaGen Hypokit must be administered by medical personnel. Onset of action after an intravenous injection of 0,2 – 0,5 mg occurs within one minute and the duration of effect is between 5 and 20 minutes. The onset of action after an intramuscular injection of 1 – 2 mg occurs after 5 – 15 minutes and lasts approximately 10 – 40 minutes.

After end of the diagnostic procedure oral carbohydrate should be given, if this is compatible with the diagnostic procedure applied.

Dosage for adult patients: The diagnostic dose for relaxation of the stomach, duodenal bulb, duodenum and small bowel is 0,2 – 0,5 mg given as intravenous injection or 1 mg given intramuscularly; the dose to relax the colon is 0,5 – 0,75 mg intravenously or 1 – 2 mg intramuscularly.

Special populations

Paediatric population (< 18 years old):

The safety and efficacy of GlucaGen Hypokit for inhibition of gastrointestinal motility in children and adolescents have not been established. No data are available.

Elderly (≥ 65 years old):

GlucaGen Hypokit can be used in elderly patients.

Renal and hepatic impairment: GlucaGen Hypokit can be used in patients with renal and hepatic impairment.

4.3 Contraindications

GlucaGen Hypokit is contra-indicated in cases of phaeochromocytoma.

Must not be administered to patients who are hypersensitive to glucagon or other excipients.

4.4 Special warnings and precautions for use

Caution should be observed when GlucaGen Hypokit is used as an adjunct in endoscopic or radiographic procedures in diabetic patients or in elderly patients with known cardiac disease.

To prevent the occurrence of hypoglycaemia, oral carbohydrates should be given to restore the liver glycogen when the patient has responded to treatment. GlucaGen Hypokit reacts antagonistically towards insulin and caution should be observed if GlucaGen Hypokit is used in patients with insulinoma or glucagonoma.

Glucagon stimulates the release of catecholamines. In the presence of phaeochromocytoma, glucagon can cause the tumour to release large amounts of catecholamines, which will cause an acute hypertensive reaction.

GlucaGen Hypokit should not be given via intravenous infusion.

GlucaGen Hypokit is not effective in patients with marked depletion of liver glycogen stores, as in starvation, adrenal insufficiency, or chronic hypoglycaemia.

Persons who have been given glucagon in connection with diagnostic procedures may experience discomfort, in particular if they have been fasting. Nausea, hypoglycaemia, and blood pressure changes have been reported in these situations. After end of a diagnostic procedure oral

carbohydrates should be given to patients who have been fasting, if this is compatible with the diagnostic procedure applied. If fasting is needed post-examination or in case of severe hypoglycaemia, glucose given intravenously may be required.

4.5 Interaction with other medicines and other forms of interaction

Insulin: Reacts antagonistically towards GlucaGen Hypokit.

Indomethacin: GlucaGen Hypokit may lose its ability to raise blood glucose or paradoxically may even produce hypoglycaemia.

Warfarin: GlucaGen Hypokit may increase the anticoagulant effect of warfarin.

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 coronary artery disease.

Interactions between GlucaGen Hypokit and other drugs are not known when GlucaGen Hypokit is used in the approved indications.

4.6 Fertility, pregnancy and lactation

Pregnancy

GlucaGen Hypokit does not cross the human placenta barrier.

GlucaGen Hypokit can be used during pregnancy.

Lactation

GlucaGen Hypokit is rapidly cleared from the bloodstream ($t_{½}$ = 3 – 6 min) thus the amount excreted in the milk of nursing mothers will be extremely small. As GlucaGen Hypokit is degraded in the digestive tract and is not

absorbed in its intact form, it will not exert any metabolic effect on the child. GlucaGen Hypokit can be used during breast-feeding.

Fertility

Animal reproduction studies have not been conducted with GlucaGen Hypokit. Studies in rats have shown that glucagon does not cause impaired fertility.

4.7 Effects on ability to drive and use machines

After a hypoglycaemic event, the patient's ability to concentrate and react may be impaired. The patient should not drive or operate machinery after a hypoglycaemic event.

After diagnostic procedures, hypoglycaemia has been reported infrequently. Therefore driving a vehicle should be avoided until the patient has had a meal with oral carbohydrates.

4.8 Undesirable effects

Summary of the safety profile

Severe adverse reactions are very rare, although nausea, vomiting and abdominal pain may occur occasionally. Hypersensitivity reactions, including anaphylactic reactions, have been reported as 'very rare' (less than 1 case per 10,000 patients).

When used in the diagnostic indication, hypoglycaemia/hypoglycaemic coma has been reported, especially in patients who have fasted. Cardiovascular adverse events, such as tachycardia and blood pressure changes have only been reported when GlucaGen Hypokit is used as an adjunct in endoscopic or radiographic procedures.

Tabulated summary of adverse reactions

Frequencies of undesirable effects considered related to GlucaGen Hypokit treatment during clinical trials and or post-marketing surveillance survey is presented in the table below. Undesirable effects that have not been observed in clinical trials but have been reported spontaneously are presented as “very rare”.

During marketed use reporting of adverse drug reactions are very rare (<1/10 000). However, post-marketing experience is subject to under reporting and this reporting rate should be interpreted in that light.

Therapeutic indication (Hypoglycaemia)

Organ system class	**Common** **≥ 1/100 and < 1/10**	**Uncommon** **≥ 1/1 000 and < 1/100**	**Rare** **≥ 1/10 000 and < 1/1 000**	**Very rare** **< 1/10 000**
Immune System disorders				Hypersensitivity reactions including anaphylactic reaction/shock
Gastrointestinal disorders	Nausea	Vomiting	Abdominal pain	

Paediatric population:

Based on data from clinical trials and post-marketing experience, the frequency, type and severity of adverse reactions observed in children are expected to be the same as in adults.

Other special populations:

Based on data from clinical trials and post-marketing experience, the frequency, type and severity of adverse reactions observed in elderly patients and in patients with renal or hepatic impairment are expected to

be the same as in the general population.

Diagnostic procedures

Organ system class	Common ≥ 1/100 and < 1/10	Uncommon ≥ 1/1 000 and < 1/100	Rare ≥ 1/10 000 and < 1/1 000	Very rare < 1/10 000
Immune System disorders				Hypersensitivity reactions including anaphylactic reaction/shock
Metabolism and nutrition disorders		Hypoglycaemia *1		Hypoglycaemic coma
Cardiac disorders				Tachycardia*2
Vascular disorders				Hypotension*2 Hypertension*2
Gastrointestinal disorders	Nausea	Vomiting	Abdominal pain	

Paediatric population:

There are no data available on the diagnostic use of GlucaGen Hypokit in children.

Other special populations:

Based on data from clinical trials and post-marketing experience, the frequency, type and severity of adverse reactions observed in elderly patients and in patients with renal or hepatic impairment are expected to be the same as in the general population.

*1 After a diagnostic procedure this could be more pronounced in patients that have fasted.

*2 Cardiovascular adverse events have only been reported when GlucaGen

Hypokit is used as an adjunct in endoscopic or radiographic procedures.

4.9 Overdose

In the case of overdose, the patient may experience nausea and vomiting. Due to the short half-life of glucagon, these symptoms will be transient.

In case of dosages substantially above the approved range, the serum potassium may decrease and should be monitored and corrected, if needed.

Treatment is symptomatic and supportive.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:

Pancreatic hormones, Glycogenolytic hormones: H04AA01

(A.21.11 Hyperglycaemic hormones)

Mechanism of action

Glucagon is a hyperglycaemic agent that mobilises hepatic glycogen, which is released into the blood as glucose. Glucagon inhibits the tone and motility of the smooth muscle in the gastrointestinal tract.

Pharmacodynamic effects

When used in treatment of severe hypoglycaemia, an effect on blood glucose is usually seen within 10 minutes.

The onset of inhibitory effect on gastrointestinal motility occurs within 1 minute after an intravenous injection. Duration of action is in the range 5 – 20 minutes depending on the dose. The onset of effect occurs within 5 –

15 minutes after an intramuscular injection, with a duration of 10 – 40 minutes depending on the dose.

5.2 Pharmacokinetic properties

Metabolism

Glucagon is degraded enzymatically in the blood plasma and in the organs to which it is distributed. The liver and kidney are major sites of glucagon clearance, each organ contributing about 30 % to the overall metabolic clearance rate.

Elimination

Glucagon has a short half-life in the blood of about 3 - 6 minutes. Metabolic clearance rate of glucagon in humans is approximately 10 ml/kg/min.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate

Water For Injections

6.2 Incompatibilities

There are no known incompatibilities with GlucaGen Hypokit.

6.3 Shelf life

24 months

6.4 Special precautions for storage

GlucaGen Hypokit should be stored at a temperature of 2 – 8 °C (in a refrigerator). Only the user can store GlucaGen Hypokit at a temperature not exceeding 25 °C for 18 months provided that the expiry date is not exceeded.

Store in the original package in order to protect from light.

Avoid freezing to prevent damage to the syringe.

If, in rare cases, the reconstituted product shows any signs of fibril formation (viscous appearance) or insoluble matter, it should be discarded.

Keep out of reach of children.

6.5 Nature and contents of container

A pack containing 1 vial of bio-synthetic glucagon as hydrochloride equivalent to glucagon 1 mg and an accompanying syringe containing 1 ml Water for Injections.

6.6 Special precautions for disposal and other handling

Reconstitution

Inject the water for injections (1,1 ml) into the vial containing the glucagon compacted powder. Shake the vial gently until the glucagon is completely dissolved and the solution is clear. Withdraw the solution back into the syringe.

Note that a syringe with a thinner needle and a finer graduation may be more suitable for use in diagnostic procedures.

The reconstituted solution appears clear and colourless and forms an injection of 1 mg (1 IU) per ml to be administered subcutaneously, intramuscularly or intravenously (injection).

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

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10 Marion Street Office Park Building

Building C1, Sandton

Johannesburg

2196

8 REGISTRATION NUMBER(S)

Y/21.11/0301

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

01 June 1993

10 DATE OF REVISION OF THE TEXT

19 May 2023