SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Ogluo 0.5 mg solution for injection in pre-filled pen.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each pre-filled pen contains 0.5 mg glucagon in 0.1 mL.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection (injection)

A clear, colourless to pale yellow solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Ogluo is indicated for the treatment of severe hypoglycaemia in adults, adolescents, and children aged 2 years and over with diabetes mellitus.

4.2 Posology and method of administration

Posology

Adults and adolescents (≥6 years)

The recommended dose is 1 mg, administrated by subcutaneous injection.

Paediatric population (≥2 to <6 years)

- The recommended dose for paediatric patients who weigh less than 25 kg is 0.5 mg administered by subcutaneous injection.

- The recommended dose for paediatric patients who weigh 25 kg or greater is 1 mg administered by subcutaneous injection.

Time to respond and additional doses

The patient will normally respond within 15 minutes. When the patient has responded to the treatment, give an oral carbohydrate to restore the liver glycogen and prevent relapse of hypoglycaemia. If the patient does not respond within 15 minutes, an additional dose of Ogluo from a new device may be administered while waiting for emergency assistance. It is recommended that patients are prescribed two Ogluo devices.

Special populations

Elderly (≥ 65 years old)

Ogluo can be used in elderly patients. No dose adjustment is required.

Efficacy and safety data are very limited in patients aged 65 years and absent in patients aged 75 and above.

Renal impairment

Ogluo can be used in patients with renal impairment. No dose adjustment is required.

Hepatic impairment

Ogluo can be used in patients with hepatic impairment. No dose adjustment is required.

Paediatric population (<2 years)

The safety and efficacy of Ogluo in children aged less than 2 years have not been established. No data are available.

Method of administration

Ogluo pre-filled pen and pre-filled syringe are for subcutaneous injection only.

Patients and their caregivers should be instructed on the signs and symptoms of severe hypoglycaemia. As severe hypoglycaemia requires the help of others to recover, the patient should be instructed to inform those around them about Ogluo and its package leaflet. Ogluo should be administered as soon as possible when severe hypoglycaemia is recognised.

The patient or caregiver should be instructed to read the package leaflet at the time they receive a prescription for Ogluo. The following instructions should be emphasised:

- The foil pouch should not be opened until glucagon needs to be administered.
- The medicinal product should be administered according to the printed instructions on the foil pouch label, carton, or the package leaflet.
- The solution should be visually inspected prior to administration. The solution should appear clear and colourless to pale yellow and be free of particles. If the solution is discoloured or contains particulate matter, the medicinal product should not be used.
- Any clothing covering the injection site should be removed. The injection should be administered in the lower abdomen, outer thigh, or outer upper arm.
- Emergency assistance should be called immediately after administering the dose, even if the patient is not unconscious.
- Each device contains a single dose of glucagon and cannot be reused.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Pheochromocytoma.

4.4 Special warnings and precautions for use

Glycogen stores and hypoglycaemia

To prevent relapse of the hypoglycaemia, oral carbohydrates should be given to restore the liver glycogen, when the patient has responded to the treatment.

Glucagon will not be effective in patients whose liver glycogen is depleted. For that reason, glucagon has little or no effect when the patient has been fasting for a prolonged period, or is suffering from adrenal insufficiency, chronic hypoglycaemia, or alcohol induced hypoglycaemia.

Glucagon, unlike adrenaline, has no effect upon muscle phosphorylase and therefore cannot assist in the transference of carbohydrate from the much larger stores of glycogen that are present in the skeletal muscle.

Insulinoma

In patients with insulinoma, 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 and cause hypoglycaemia. A patient developing symptoms of hypoglycaemia after a dose of glucagon should be given glucose orally or intravenously.

Caution should also be observed in patients with glucagonoma.

Recovery time

Please take into account that approximately 15% of patients achieved glucose recovery after 20 minutes or more in the pivotal trial.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

Insulin

Insulin reacts antagonistically towards glucagon.

Indomethacin

When used with indomethacin, glucagon may lose its ability to raise blood glucose or paradoxically, may even produce hypoglycaemia.

Warfarin

Glucagon 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.

4.6 Fertility, Pregnancy and lactation

Pregnancy

Glucagon does not cross the human placenta barrier. The use of glucagon has been reported in pregnant women with diabetes and no harmful effects are known with respect to the course of pregnancy and the health of the unborn and the neonate. Ogluo can be used during pregnancy.

Breast feeding

Glucagon is cleared from the bloodstream very fast (mainly by the liver) (t1/2= 3–6 minutes); thus the amount excreted in the milk of breast-feeding mothers following treatment of severe hypoglycaemic reactions is expected to be extremely small. As glucagon is degraded in the digestive tract and cannot be absorbed in its intact form, it will not exert any metabolic effect in the child. Ogluo can be used during breast feeding.

Fertility

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

4.7 Effects on ability to drive and use machines

Ogluo has negligible influence on the ability to drive and use machines.

After a severe hypoglycaemic event, the patient's ability to concentrate and react may be impaired; therefore the patient should not drive or operate machinery after a severe hypoglycaemic event until the patient has stabilised.

4.8 Undesirable effects

Summary of the safety profile

The most frequently reported adverse reactions are nausea (30%) and vomiting (16%).

Tabulated list of adverse reactions

Frequencies of adverse reactions considered related to treatment with Ogluo during clinical trials are presented below. The adverse drug reactions are classified according to the System Organ Class. Frequency groups are defined by the following convention: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000), and not known (cannot be estimated from available data). Within each frequency group, adverse reactions are presented in order of decreasing seriousness

Table 1. Frequency of adverse reactions of glucagon injection

System organ class	Subject incidence	Adverse drug reaction
Nervous system disorders	Common	Headache
Cardiac disorders	Common	Tachycardia
Gastrointestinal disorders	Very common	Vomiting
	Very common	Nausea
	Common	Diarrhoea
	Uncommon	Abdominal pain
General disorders and administration site conditions	Common	Injection site pain
	Common	Injection site oedema
	Uncommon	Injection site bruising
	Uncommon	Injection site erythema

Description of selected adverse reactions

The most frequently reported adverse reactions are nausea (43%), vomiting (13%), and headache (5%). Adverse reactions are mild to moderate in severity and resolved on their own. No serious adverse reactions have been related to glucagon.

Hypersensitivity reactions, including anaphylactic reactions, have been reported as ‘very rare’ (<1/10,000 patients) with injectable glucagon. These are known medicinal product class effects of glucagon.

Paediatric population

The most frequently reported adverse reactions are nausea (48%), vomiting (19%), hyperglycaemia (7%), and headache (7%). Hypoglycaemia (42%) was observed in clinical trials but was not considered related to glucagon. The most frequently reported adverse reactions observed by age group are presented below.

Table 2. Frequency of most common adverse reactions among paediatric populations

	Ages 2 to under 6 years of age (0.5 mg dose) N =7	Ages 6 to under 12 years of age (0.5 mg dose) N = 13	Ages 12 to under 18 (0.5 mg dose) N = 11	Ages 12 to under 18 (1 mg dose) N = 11
Nausea	43%	54%	36%	36%
Vomiting	14%	23%	0%	18%
Hyperglycaemia	14%	8%	0%	0%
Headache	0%	15%	0%	0%

Other special populations

Efficacy and safety data for Ogluo are very limited in patients aged 65 years and absent in patients aged 75 and above, in or pregnant patients, or patients with hepatic or renal impairment. Based upon 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.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Yellow Card Scheme, Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

If overdose occurs, the patient may experience nausea, vomiting, inhibition of gastro-intestinal tract motility, increase in blood pressure and pulse rate. In case of suspected overdosing, serum potassium may decrease and should be monitored and corrected if needed. If the patient develops a dramatic increase in blood pressure, use of non-selective α-adrenergic blockade has been shown to be effective in lowering blood pressure for the short time that control would be needed (see section **Error! Reference source not found.**).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Pancreatic hormones, glycogenolytic hormones: H04AA01.

Mechanism of action

Glucagon is a hyperglycaemic agent that mobilises hepatic glycogen, which is released into the blood as glucose. Hepatic stores of glycogen are necessary for glucagon to produce an anti-hypoglycaemic effect.

Pharmacodynamic effects

After administration of 1 mg Ogluo in adult patients with diabetes, the mean maximum plasma glucose increase from baseline was 176 mg/dL. After administration, plasma glucose begins to rise as early as 5 minutes. From the time of injection, the mean time to plasma glucose >70 mg/dL or ≥20 mg/dL increase was 14.8 (±5.3) minutes.

Clinical efficacy and safety

Ogluo was evaluated in 132 adult patients aged 18 to 74 years with type 1 diabetes in a multicentre randomised, active-controlled, single-blind, 2-way crossover study. The study involved 2 clinic visits 7 to 28 days apart, with random assignment to receive glucagon 1 mg solution for injection during one session and reconstituted glucagon 1 mg powder and solvent for solution for injection during the other. A total of 127 subjects received an injection of Ogluo and 123 subjects received a glucagon powder and solvent for solution for injection.

The efficacy of glucagon 1 mg solution for injection was compared to reconstituted glucagon 1 mg powder and solvent for solution for injection in subjects who were in a state of insulin-induced hypoglycaemia with target plasma glucose less than 3.0 mmol/L (<54 mg/dL). Treatment ‘success’ was defined as plasma glucose increase from time of glucagon administration to absolute value greater than 3.89 mmol/L (>70 mg/dL) or relative increase of 1.11 mmol/L (≥20 mg/dL) or greater, within 30 minutes after glucagon administration. The proportion of patients who achieved treatment ‘success’ was 99.2% in the glucagon 1 mg solution for injection group and 100% in the reconstituted glucagon 1 mg powder and solvent for solution for injection group, and the comparison between groups met the prespecified non-inferiority margin.

From the time of administration, which does not include the preparation time for each medicinal product prior to administration the mean time to treatment ‘success’ was 14.8 (±5.3) minutes in the glucagon 1 mg solution for injection group and 10.4 (±1.8) minutes in the reconstituted glucagon 1 mg powder and solvent for solution for injection group.

From the time of decision to dose, which includes the preparation time for each medicinal product prior to administration, the mean time to treatment ‘success’ was 15.6 (±5.2) minutes in the glucagon 1 mg solution for injection group and 12.2 (±2.0) minutes in the reconstituted glucagon 1 mg powder and solvent for solution for injection.

Paediatric population

Ogluo was evaluated in 31 pediatric patients ages 2 to 18 years (7 patients in the 2-<6, 13 patients in the 6-<12 and 11 patients in the 12-<18 years old group) with T1DM in an open-label, sequential, uncontrolled clinical study. Efficacy was assessed based on increases from Baseline in mean plasma glucose 30 minutes post-dosing. Statistically significant changes from Baseline of 81.4 mg/dL [SD=18.3], 84.2 mg/dL [SD=25.3], and 54.0 mg/dL [SD=27.3] were observed in the 2-< 6 years, 6-<12 years,

and 12-< 18 years [1 mg dose] age groups, respectively). Across all 31 subjects the mean time to plasma glucose increase ≥25 mg/dL from baseline was 18.9 minutes.

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

5.2 Pharmacokinetic properties

Absorption

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

Distribution

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

Metabolism

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

Elimination

The mean half-life of Ogluo was determined to be 31.9 ± 9.13 minutes.

Paediatric population

Subcutaneous injection of 0.5 mg Ogluo in subjects with type 1 diabetes mellitus ages 2 to under 6 years resulted in a mean glucagon C_{max} of 2 300 pg/mL, t_{max} of 41 minutes, and $AUC_{0\text{-}180min}$ of 138 900 pg/mL*min. Subcutaneous injection of 0.5 mg Ogluo in subjects with type 1 diabetes mellitus ages 6 to under 12 years resulted in a mean C_{max} of 1 600 pg/mL, median t_{max} of 34 minutes and $AUC_{0\text{-}180min}$ of 104 700 pg/mL*min. Subcutaneous injection of 1 mg Ogluo in subjects with type 1 diabetes mellitus ages 12 to less than 18 years resulted in a mean C_{max} of 1 900 pg/mL, t_{max} of 51 minutes $AUC_{0\text{-}180min}$ of 134 300 pg/mL*min.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Trehalose Dihydrate

Dimethyl sulfoxide (DMSO)

Sulfuric Acid

Water for injections

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 25°C.

Do not refrigerate or freeze. Do not store below 15°C.

Store in original sealed foil pouch until time of use in order to protect from light and moisture.

6.5 Nature and contents of container

A pre-filled, single-dose pen containing a 1 mL cyclic olefin polymer syringe with ETFE coated chlorobutyl rubber piston, 27-gauge staked stainless steel needle,bromo butyl rubber flexible needle shield, and a red cap.

Each pre-filled pen contain 0.1 mL of solution for injection and is individually packaged in a predominantly red-coloured foil pouch, in a red on white carton displaying a pre-filled pen image.

Pack sizes of one and two single-dose pre-filled pens.

6.6 Special precautions for disposal

This is a ready to use medicinal product and for single-use only.

The single-dose device contains only one dose.

The instructions for using the medicinal product in the package leaflet must be followed carefully.

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

7 MARKETING AUTHORISATION HOLDER

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D02 T292,
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8 MARKETING AUTHORISATION NUMBER(S)

PL 56910/0001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

23/04/2021

10 DATE OF REVISION OF THE TEXT

30/09/2025