

Indication	<p>Management of neonatal hypoglycaemia:</p> <ul style="list-style-type: none"> • Refractory to intravenous glucose infusions • When glucose infusion is unavailable <p>Management of hyperinsulinaemic hypoglycaemia (e.g. congenital hyperinsulinism). Adjunctive treatment of beta-blocker overdose.</p>												
Action	Stimulates hepatic gluconeogenesis and glycogenolysis. Glucagon has a positive inotropic action.												
Drug type	Polypeptide hormone – hyperglycaemic agent												
Trade name	GlucaGen HypoKit 1 mg/mL												
Presentation	1 mg/mL vial. 1 unit of glucagon = 1 mg (1000 microgram) glucagon												
Dose	<p>IV bolus/IM/SC 200 microgram/kg/dose. Do not exceed 1 mg/dose. IV glucose is to be administered as soon as possible.</p> <p>IV infusion 5–20 microgram/kg/hour. Consider starting dose of 20 microgram/kg/hour and decrease carefully, monitoring blood glucose, until the minimum effective dose is reached.</p> <p>Beta-blocker overdose: Refer to evidence summary.</p>												
Dose adjustment	<p>Therapeutic hypothermia – No information. ECMO – NO information. Renal impairment – No information. Hepatic impairment – No information.</p>												
Maximum dose	Maximum stat dose: 1 mg (1000 microgram)												
Route	IV, IM, SC												
Preparation	<p>IV bolus/IM/SC: Reconstitute 1 mg (1000 microgram) glucagon vial with 1 mL of diluent provided (water for injection) to make a 1 mg/mL (1000 microgram/mL) solution.</p> <p>IV infusion: Note: Refer to Appendix for tables to assist with concentration selection.</p> <p>Weight suggestions for infusion concentrations below are a guide only. Clinicians may choose infusion concentration different to the suggested based on expected dose and the corresponding 24-hour fluid volumes</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="text-align: left;">Infant weight</th> <th style="text-align: center;">≤1kg</th> <th style="text-align: center;">1 to 2.5kg</th> <th style="text-align: center;">≥2.5kg</th> </tr> </thead> <tbody> <tr> <td style="text-align: left;">Suggested glucagon concentration</td> <td style="text-align: center;">40 microgram/mL</td> <td style="text-align: center;">80 microgram/mL</td> <td style="text-align: center;">160 microgram/mL</td> </tr> <tr> <td style="text-align: left;">10 microgram/kg/hour is equal to</td> <td style="text-align: center;">0.25 mL/kg/hour</td> <td style="text-align: center;">0.125 mL/kg/hour</td> <td style="text-align: center;">0.0625 mL/kg/hour</td> </tr> </tbody> </table>	Infant weight	≤1kg	1 to 2.5kg	≥2.5kg	Suggested glucagon concentration	40 microgram/mL	80 microgram/mL	160 microgram/mL	10 microgram/kg/hour is equal to	0.25 mL/kg/hour	0.125 mL/kg/hour	0.0625 mL/kg/hour
Infant weight	≤1kg	1 to 2.5kg	≥2.5kg										
Suggested glucagon concentration	40 microgram/mL	80 microgram/mL	160 microgram/mL										
10 microgram/kg/hour is equal to	0.25 mL/kg/hour	0.125 mL/kg/hour	0.0625 mL/kg/hour										

20mL Syringe

Reconstitution: Add 1 mL of diluent provided (water for injection) to the 1 mg vial (1000 microgram) of glucagon to make a **1 mg/mL (1000 microgram/mL) solution**.

It is a 2-step dilution for the 40 microgram/mL solution only. It is a 1-step dilution for the 80 and 160 microgram/mL concentrations.

Step 1: Draw up glucagon reconstitution and add compatible fluid* to make a diluted solution as per table below:

Glucagon concentration	40 microgram/mL	80 microgram/mL	160 microgram/mL
Volume of glucagon reconstitution (1 mg/mL)	1 mL (1 mg)	1.6 mL (1.6 mg)	3.2 mL (3.2 mg)
Volume of compatible fluid*	4 mL	18.4 mL	16.8 mL
Total volume	5 mL (200 microgram/mL)	20 mL	20 mL

Step 2: Draw up diluted glucagon and add compatible fluid* as per table below to make a final volume of 20 mL

Glucagon concentration	40 microgram/mL
Volume of diluted glucagon from step 1	4 mL (800 microgram)
Volume of compatible fluid*	16 mL
Total volume	20 mL

* Compatible fluid: glucose 5%

50mL Syringe

Reconstitution: Add 1 mL of diluent provided (water for injection) to the 1 mg vial (1000 microgram) of glucagon to make a **1 mg/mL (1000 microgram/mL) solution**.

Draw up reconstituted glucagon and add compatible fluid* as per table below to make a final volume of 50 mL

Glucagon concentration	40 microgram/mL	80 microgram/mL	160 microgram/mL
Volume of glucagon (1 mg/mL)	2 mL (2 mg)	4 mL (4 mg)	8 mL (8 mg)
Volume of compatible fluid*	48 mL	46 mL	42 mL
Total volume	50 mL	50 mL	50 mL

* Compatible fluid: glucose 5%

Administration	Do not use the reconstituted solution unless it is clear. IV bolus: Administer 0.2 mL/kg of the reconstituted solution (to a maximum 1 mL) over 3 to 5 minutes. IM: Inject into the anterolateral thigh (preferred) or the ventrogluteal areas. ^{1,2} SC: Inject into the area over the deltoid muscle or over the anterolateral thigh. ^{1,3} Continuous IV infusion: Via syringe driver.
Monitoring	Blood glucose concentrations, watch for rebound hypoglycaemia after cessation. Consider cardiorespiratory and blood pressure monitoring. Electrolytes for continuous infusion.
Contraindications	Phaeochromocytoma ⁴⁻⁶ , glucagonoma. Hypersensitivity to glucagon or any component.
Precautions	Hypertension. Insulinoma: Glucagon has been used to treat hypoglycaemia caused by insulinoma. However, it should be used cautiously because of the propensity to release insulin. ⁷
Drug interactions	Drug interactions largely unreported in newborn infants. Glucagon has a positive inotropic action which may counteract effect of beta-blockers. Beta-blockers may reduce hyperglycaemic effect of glucagon. ⁸ Warfarin: Increased effect of warfarin resulting in increased risk of bleeding. ⁹

	Indomethacin: Glucagon may lose its ability to raise blood glucose or paradoxically may even produce hypoglycaemia. ⁷
Overdose	AUSTRALIA: Contact the Poisons Information Centre on 13 11 26 for management NEW ZEALAND: Contact the National Poisons Centre on 0800 764 766 for management
Adverse reactions	Generally well tolerated. Transient increase in blood pressure and pulse rate. ⁷ Anaphylaxis or hypersensitivity reactions have been reported in adults. ⁷ Very rare: Hypertension, hypotension, vomiting. ⁷ Erythema necrolyticum migrans (erythematous squamous skin lesions) has been reported with prolonged glucagon infusion.
Compatibility	Fluids: Glucose 5%. ²¹ PN at Y-site: No information Y-site: naloxone.
Incompatibility	Fluids: Solutions that contain calcium. PN at Y-site: No information Y-site: No information.
Stability	Discard any unused solution. Continuous IV infusion should be used within 24 hours
Storage	Store below 25°C. Do not freeze. The sealed container should be protected from light.
Excipients	Lactose monohydrate, hydrochloric acid (for pH adjustment), sodium hydroxide (for pH adjustment), and water for injections.
Evidence	Efficacy Treatment of hypoglycaemia: The data are mainly derived from case series and case reports. ¹⁰⁻¹³ A single bolus dose of glucagon (200 microgram/kg) caused a rapid rise in hepatic glucose production rate in newborns with hypoglycaemia. ¹² (LOE IV) Glucagon infusion (0.5–1 mg/day = 20–40 microgram/hour) resulted in a significant rise in blood glucose concentration within 4 hours of infusion in newborn infants irrespective of the cause of hypoglycaemia. ¹³ (LOE IV, GOR C). Glucose production in response to a glucagon 100 microgram/kg bolus was comparable in preterm, Appropriately Grown for Age and Small for Gestational Age infants. ¹⁴ (LOE IV). Glucagon infusion (20–40 microgram/hour) has been used to treat refractory hypoglycaemia in sick preterm infants (mean birth weight 1814 g and gestational age 32 weeks). ¹¹ (LOE IV) Treatment of low-output heart failure associated with beta-blocker overdose: A case report of a preterm infant with low output heart failure after maternal labetalol use who responded to repeated use of intravenous glucagon 0.3 to 0.6 mg/kg. ¹⁵ (LOE IV GOR C). This is consistent with doses in case reports of glucagon use for adult beta-blocker overdose. ¹⁶ Safety Hyponatraemia has been variably reported with glucagon infusion ^{13,17,18} although it may be explained by other factors including glucose infusion. (LOE IV GOR D) Thrombocytopenia has been reported ^{13,17} although a case series found increasing platelet counts during infusion. ¹¹ Erythema necrolyticum migrans (erythematous squamous skin lesions) has been reported with prolonged glucagon infusion. ^{19,20} Glucagon has been reported to induce hypertension in patients with pheochromocytoma. ^{8,10,11} Adverse cardiovascular events attributable to glucagon have not been reported in newborns. Pharmacodynamics An effect on blood glucose is usually seen within 5–20 minutes after IV, IM or SC administration. ¹¹ Response to an intravenous bolus persists for at least 45 minutes. ¹³ Pharmacokinetics Adult data report half-life of 8–18 minutes. ⁷
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Appendix

Infusion tables to assist concentration selection

Table 1: Infusion rates when using glucagon concentration **40 microgram/mL**
(suggested for weight <1kg)

Rate (mL/hr)	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
Weight (kg)	Approximate micrograms/kg/hour									
0.5	8	16	24	32	40	48	56	64	72	80
1	4	8	12	16	20	24	28	32	36	40
1.5	2.7	5.3	8	11	13	16	18	21	24	27
2	2	4	6	8	10	12	14	16	18	20
2.5	1.6	3.2	4.8	6.4	8	9.6	11	13	14	16
3	1.3	2.7	4	5.3	6.7	8	9.3	11	12	13
3.5	1.1	2.3	3.4	4.6	5.7	6.9	8	9.1	10	11
4	1	2	3	4	5	6	7	8	9	10
4.5	0.9	1.8	2.7	3.6	4.4	5.3	6.2	7.1	8	8.9
5	0.8	1.6	2.4	3.2	4	4.8	5.6	6.4	7.2	8

Table 2: Infusion rates when using glucagon concentration **80 microgram/mL**
(suggested for weight 1 to 2.5kg)

Rate (mL/hr)	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
Weight (kg)	Approximate micrograms/kg/hour									
0.5	16	32	48	64	80	96	112	128	144	160
1	8	16	24	32	40	48	56	64	72	80
1.5	5.3	11	16	21	27	32	37	43	48	53
2	4	8	12	16	20	24	28	32	36	40
2.5	3.2	6.4	9.6	13	16	19	22	26	29	32
3	2.7	5.3	8	11	13	16	19	21	24	27
3.5	2.3	4.6	6.9	9.1	11	14	16	18	21	23
4	2	4	6	8	10	12	14	16	18	20
4.5	1.8	3.6	5.3	7.1	8.9	11	12	14	16	18
5	1.6	3.2	4.8	6.4	8	10	11	13	14	16

Table 3: Infusion rates when using glucagon concentration **160 microgram/mL** (suggested for weight >2.5kg)

Rate (mL/hr)	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
Weight (kg)	Approximate micrograms/kg/hour									
0.5	32	64	96	128	160	192	224	256	288	320
1	16	32	48	64	80	96	112	128	144	160
1.5	11	21.3	32	43	53	64	75	85	96	107
2	8	16	24	32	40	48	56	64	72	80
2.5	6.4	13	19	26	32	38	45	51	58	64
3	5.3	11	16	21	27	32	37	43	48	53
3.5	4.6	9.1	14	18	23	27	32	37	41	46
4	4	8	12	16	20	24	28	32	36	40
4.5	3.6	7.1	11	14	18	21	25	28	32	36
5	3.2	6.4	9.6	13	16	19	22	26	29	32

$$\text{Rate (mL/hr)} = \frac{\text{Dose (microgram/kg/hour)} \times \text{Weight (kg)}}{\text{Concentration (microgram/mL)}}$$

$$\text{Dose (microgram/kg/hour)} = \frac{\text{Rate (mL/hr)} \times \text{Concentration (microgram/mL)}}{\text{Weight (kg)}}$$

VERSION/NUMBER	DATE
Original 1.0	27/02/2026
REVIEW	27/02/2031

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