

Alert									
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)								
Total cumulative dose									
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 SINGLE STRENGTH infusion:</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 50%;">Infusion Strength</th> <th style="width: 50%;">Prescribed amount</th> </tr> </thead> <tbody> <tr> <td>1 mL/hour = 10 microgram/kg/hour</td> <td>0.5 mg/kg (0.5 mL/kg) glucagon to make up to 50 mL</td> </tr> </tbody> </table> <p>Add 1 mL of diluent provided (water for injection) to the 1 mg vial (1000 microgram of glucagon) to make a 1mg/mL solution. FURTHER DILUTE Draw up 0.5 mL/kg (0.5 mg/kg of glucagon) of the above solution and make up to a final volume of 50 mL with glucose 5% to make a final concentration of 10 microgram/kg/mL. Infusing at 1 mL/hour = 10 microgram/kg/hour.</p> <p>DOUBLE STRENGTH infusion</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 50%;">Infusion Strength</th> <th style="width: 50%;">Prescribed amount</th> </tr> </thead> <tbody> <tr> <td>1 mL/hour = 20 microgram/kg/hour</td> <td>1 mg/kg (1 mL/kg) glucagon to make up to 50 mL</td> </tr> </tbody> </table> <p>Add 1 mL of diluent provided (water for injection) to the 1 mg vial (1000 microgram of glucagon) to make a 1mg/mL solution. FURTHER DILUTE Draw up 1 mL/kg (1 mg/kg of glucagon) of the above solution and make up to a final volume of 50 mL with glucose 5% to make a final concentration of 20 microgram/kg/mL. Infusing at 1 mL/hour = 20 microgram/kg/hour.</p>	Infusion Strength	Prescribed amount	1 mL/hour = 10 microgram/kg/hour	0.5 mg/kg (0.5 mL/kg) glucagon to make up to 50 mL	Infusion Strength	Prescribed amount	1 mL/hour = 20 microgram/kg/hour	1 mg/kg (1 mL/kg) glucagon to make up to 50 mL
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Administration	<p>Do not use the reconstituted solution unless it is clear.</p> <p>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.</p>								

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].
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% and 10%, sodium chloride 0.9%. Y-site: Naloxone.
Incompatibility	Fluids: Solutions that contain calcium. Y-site: No information.
Stability	Discard any unused solution. IV infusion solution is stable for 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.
Special comments	
Evidence	<p>Efficacy</p> <p>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)</p> <p>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].</p> <p>Safety</p> <p>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 phaeochromocytoma [8, 10, 11]. Adverse cardiovascular events attributable to glucagon have not been reported in newborns.</p> <p>Pharmacodynamics</p> <p>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].</p> <p>Pharmacokinetics</p> <p>Adult data report half-life of 8–18 minutes.[7]</p>

Practice points	
References	<ol style="list-style-type: none"> 1. The Australian Immunisation Handbook 10th edition 2013 (updated January 2014). 2. Rishovd A. Pediatric intramuscular injections: guidelines for best practice. <i>MCN Am J Matern Child Nurs.</i> 2014;39:107-12; quiz 13-4. 3. Hensel D, Morson GL, Preuss EA. Best practices in newborn injections. <i>MCN Am J Matern Child Nurs.</i> 2013;38:163-7; quiz 8-9. 4. Hosseinneshad A, Black RM, Aeddula NR, Adhikari D, Trivedi N. Glucagon-induced pheochromocytoma crisis. <i>Endocr Pract.</i> 2011;17:e51-4. 5. Minamori Y, Yamamoto M, Tanaka A, Takeda N, Yasuda K. Hazard of glucagon test in diabetic patients. Hypertensive crisis in asymptomatic pheochromocytoma. <i>Diabetes Care.</i> 1992;15:1437-8. 6. Sebel EF, Hull RD, Kleerekoper M, Stokes GS. Responses to glucagon in hypertensive patients with and without pheochromocytoma. <i>Am J Med Sci.</i> 1974;267:337-43. 7. Product Information: GlucaGen(R) intramuscular injection, intravenous injection, subcutaneous injection, glucagon rDNA origin intramuscular injection, intravenous injection, subcutaneous injection. Boehringer Ingelheim Pharmaceuticals, Inc. (per DailyMed), Ridgefield, CT, 2014. 8. Messerli FH, Kuchel O, Tolis G, Hamet P, Fraysse J, Genest J. Effects of beta-adrenergic blockade on plasma cyclic AMP and blood sugar responses to glucagon and isoproterenol in man. <i>Int J Clin Pharmacol Biopharm.</i> 1976;14:189-94. 9. Micromedex solutions. Glucagon. Accessed on 22 March 2017. 10. Carter PE, Lloyd DJ, Duffty P. Glucagon for hypoglycaemia in infants small for gestational age. <i>Arch Dis Child.</i> 1988;63:1264-6. 11. Charsha DS, McKinley PS, Whitfield JM. Glucagon infusion for treatment of hypoglycemia: efficacy and safety in sick, preterm infants. <i>Pediatrics.</i> 2003;111:220-1. 12. Hawdon JM, Aynsley-Green A, Ward Platt MP. Neonatal blood glucose concentrations: metabolic effects of intravenous glucagon and intragastric medium chain triglyceride. <i>Arch Dis Child.</i> 1993;68:255-61. 13. Miralles RE, Lodha A, Perlman M, Moore AM. Experience with intravenous glucagon infusions as a treatment for resistant neonatal hypoglycemia. <i>Archives of Pediatrics & Adolescent Medicine.</i> 2002;156:999-1004. 14. van Kempen AA, Ackermans MT, Endert E, Kok JH, Sauerwein HP. Glucose production in response to glucagon is comparable in preterm AGA and SGA infants. <i>Clin Nutr.</i> 2005;24:727-36. 15. Stevens TP, Guillet R. Use of glucagon to treat neonatal low-output congestive heart failure after maternal labetalol therapy. <i>J Pediatr.</i> 1995;127:151-3. 16. Boyd R, Ghosh A. Towards evidence based emergency medicine: best BETs from the Manchester Royal Infirmary. Glucagon for the treatment of symptomatic beta blocker overdose. <i>Emerg Med J.</i> 2003;20:266-7. 17. Belik J, Musey J, Trussell RA. Continuous infusion of glucagon induces severe hyponatremia and thrombocytopenia in a premature neonate. <i>Pediatrics.</i> 2001;107:595-7. 18. Coulthard MG, Hey EN. Glucagon is very unlikely to have caused hyponatremia. <i>Pediatrics.</i> 2002;109:985. 19. Mohnike K, Blankenstein O, Pfuetzner A, Potzsch S, Schober E, Steiner S, Hardy OT, Grimberg A, van Waarde WM. Long-term non-surgical therapy of severe persistent congenital hyperinsulinism with glucagon. <i>Horm Res.</i> 2008;70:59-64. 20. Wald M, Lawrenz K, Luckner D, Seimann R, Mohnike K, Schober E. Glucagon therapy as a possible cause of erythema necrolyticum migrans in two neonates with persistent hyperinsulinaemic hypoglycaemia. <i>Eur J Pediatr.</i> 2002;161:600-3.

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