Glucagon
Newborn Use Only

### Alert
Management of neonatal hypoglycaemia:
- Refractory to intravenous glucose infusions;
- When glucose infusion is unavailable.
Management of hyperinsulinaemic hypoglycaemia (e.g. congenital hyperinsulinism).
Adjunctive treatment of beta-blocker overdose.

### Action
Glucagon 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

### Dosage/Interval

<table>
<thead>
<tr>
<th>Route</th>
<th>IV bolus/IM/SC:</th>
<th>IV infusion:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>200 microgram/kg/dose. Do not exceed 1 mg/dose. IV glucose is to be administered as soon as possible.</td>
<td>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.</td>
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<td></td>
<td><strong>Beta-blocker overdose:</strong> Refer to evidence summary.</td>
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<tr>
<td>Maximum Dose</td>
<td>Maximum stat dose: 1 mg (1000 microgram)</td>
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</table>

### Preparation/Dilution

<table>
<thead>
<tr>
<th>Infusion rate</th>
<th>Prescribed amount</th>
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</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>

Add 1 mL of diluent provided (WFI) to the 1 mg vial (1000 microgram of glucagon). Draw up 0.5 mL/kg (0.5 mg/kg of glucagon) and make up to a final volume of 50 mL with glucose 5% with a concentration of 10 microgram/kg/mL.

**Infusing at 1 mL/hour = 10 microgram/kg/hour.**

<table>
<thead>
<tr>
<th>Infusion rate</th>
<th>Prescribed amount</th>
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<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>
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</table>

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**Infusing at 1 mL/hour = 20 microgram/kg/hour.**

### 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). Consider cardiorespiratory and blood pressure monitoring.
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<table>
<thead>
<tr>
<th>Electrolytes (for continuous infusion).</th>
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<tr>
<td><strong>Contraindications</strong></td>
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<tr>
<td>Phaeochromocytoma [4-6], glucagonoma.</td>
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<tr>
<td>Hypersensitivity to glucagon or any component.</td>
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<tr>
<td><strong>Precautions</strong></td>
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<tr>
<td>Hypertension.</td>
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<tr>
<td>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].</td>
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<tr>
<td><strong>Drug Interactions</strong></td>
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<tr>
<td>Drug interactions largely unreported in newborn infants.</td>
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<tr>
<td>Glucagon has a positive inotropic action which may counteract effect of beta-blockers. Beta-blockers may reduce hyperglycaemic effect of glucagon [8].</td>
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<td>Warfarin: Increased effect of warfarin resulting in increased risk of bleeding.[9]</td>
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<tr>
<td>Indomethacin: Glucagon may lose its ability to raise blood glucose or paradoxically may even produce hypoglycaemia [7].</td>
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<tr>
<td><strong>Adverse Reactions</strong></td>
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<tr>
<td>Generally well tolerated.</td>
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<tr>
<td>Transient increase in blood pressure and pulse rate. [7]</td>
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<tr>
<td>Anaphylaxis or hypersensitivity reactions have been reported in adults. [7]</td>
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<tr>
<td>Very rare: Hypertension, hypotension, vomiting. [7]</td>
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<tr>
<td>Erythema necrolyticum migrans (erythematousquamous skin lesions) has been reported with prolonged glucagon infusion.</td>
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<tr>
<td><strong>Compatibility</strong></td>
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<tr>
<td>Fluids: Glucose 5% and 10%, sodium chloride 0.9%.</td>
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<tr>
<td>Y-site: Naloxone.</td>
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<tr>
<td><strong>Incompatibility</strong></td>
</tr>
<tr>
<td>Fluids: Solutions that contain calcium. Y-site: No information.</td>
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<tr>
<td><strong>Stability</strong></td>
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<tr>
<td>Discard any unused solution.</td>
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<tr>
<td>iV infusion solution is stable for 24 hours.</td>
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<tr>
<td><strong>Storage</strong></td>
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<tr>
<td>Store below 25°C. Do not freeze. The sealed container should be protected from light.</td>
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<tr>
<td><strong>Special Comments</strong></td>
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<tr>
<td>Evidence summary</td>
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<tr>
<td><strong>Efficacy</strong></td>
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<tr>
<td>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)</td>
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<tr>
<td>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].</td>
</tr>
<tr>
<td>Safety</td>
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<tr>
<td>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)</td>
</tr>
<tr>
<td>Thrombocytopenia has been reported [13, 17] although a case series found increasing platelet counts during infusion [11]. Erythema necrolyticum migrans (erythematosquamous 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.</td>
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<tr>
<td>Pharmacodynamics</td>
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<tr>
<td>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].</td>
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<tr>
<td>Pharmacokinetics</td>
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<tr>
<td>Adult data report half-life of 8–18 minutes.[7]</td>
</tr>
</tbody>
</table>
References