### 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.**

### Indication

- IV bolus/IM/SC: 200 microgram/kg/dose. Do not exceed 1 mg/dose. IV glucose is to be administered as soon as possible.

- **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.

**Beta-blocker overdose:** Refer to evidence summary.

### 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

#### IV bolus/IM/SC:

- **Prescribed amount:** 10 microgram/kg/hour for 1 mL/hour.

#### IV infusion:

- **SINGLE STRENGTH infusion:**
  - Infusion rate: 1 mL/hour = 10 microgram/kg/hour
  - Prescribed amount: 0.5 mg/kg (0.5 mL/kg) glucagon to make up to 50 mL
  - Add 1 mL of diluent provided (WFI) to the 1 mg (1000 microgram) vial. 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.**

- **DOUBLE STRENGTH infusion**
  - Infusion rate: 1 mL/hour = 20 microgram/kg/hour
  - Prescribed amount: 1 mg/kg (1 mL/kg) glucagon to make up to 50 mL
  - Add 1 mL of diluent provided (WFI) to the 1 mg vial (1000 microgram of glucagon). Draw up 1 mL/kg (1 mg/kg of glucagon) and make up to a final volume of 50 mL with glucose 5% with a concentration of 20 microgram/kg/mL.
  - **Infusing at 1 mL/hour = 20 microgram/kg/hour.**

### Route

**IV, IM, SC**

### Maximum Dose

**Maximum stat dose:** 1 mg (1000 microgram)

### Preparation/Dilution

#### IV bolus/IM/SC:

Add 1 mL of diluent provided (WFI) to the 1 mg (1000 microgram) vial to make a volume of 1 mL with a concentration of 1 mg/mL (1000 microgram/mL)

#### IV infusion

- **SINGLE STRENGTH infusion:**
  - Infusion rate: 1 mL/hour = 10 microgram/kg/hour
  - Prescribed amount: 0.5 mg/kg (0.5 mL/kg) glucagon to make up to 50 mL
  - Add 1 mL of diluent provided (WFI) to the 1 mg (1000 microgram) vial. 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.
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- **DOUBLE STRENGTH infusion**
  - Infusion rate: 1 mL/hour = 20 microgram/kg/hour
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  - Add 1 mL of diluent provided (WFI) to the 1 mg vial (1000 microgram of glucagon). Draw up 1 mL/kg (1 mg/kg of glucagon) and make up to a final volume of 50 mL with glucose 5% with a concentration of 20 microgram/kg/mL.
  - **Infusing at 1 mL/hour = 20 microgram/kg/hour.**

### Administration

- Do not use the reconstituted solution unless it is clear.
- **IV bolus:** Administer 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.
- Electrolytes (for continuous infusion).
<table>
<thead>
<tr>
<th>Contraindications</th>
<th>Phaeochromocytoma [4-6], glucagonoma. Hypersensitivity to glucagon or any component.</th>
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<tbody>
<tr>
<td>Precautions</td>
<td>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].</td>
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<tr>
<td>Drug Interactions</td>
<td>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].</td>
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<tr>
<td>Adverse Reactions</td>
<td>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 (erythematousquamous skin lesions) has been reported with prolonged glucagon infusion.</td>
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<tr>
<td>Compatibility</td>
<td>Fluids: Glucose 5% and 10%, sodium chloride 0.9%. Y-site: Naloxone.</td>
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<tr>
<td>Incompatibility</td>
<td>Fluids: Solutions that contain calcium. Y-site: No information.</td>
</tr>
<tr>
<td>Stability</td>
<td>Discard any unused solution. IV infusion solution is stable for 24 hours.</td>
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<td>Storage</td>
<td>Store below 25°C. Do not freeze. The sealed container should be protected from light.</td>
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<td>Special Comments</td>
<td>Evidence summary: 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 (erythematousquamous 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. 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]</td>
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References