Insulin for Hyperkalaemia
Newborn Use Only

2019

Alert	High risk of hyperglycaemia and hypoglycaemia. Insulin binds to the plastic of giving sets. Flush the plastic tubing with 20 mL of prepared insulin solution into a receptacle prior to connecting to the infant. This is to saturate the binding. Insulin concentrations ≤ 0.05 units/mL are not reliably delivered even after preconditioning and flushing.
Indication	Treatment of hyperkalaemia: • Infants with serum potassium (K^+) ≧ 7.0 mmol/L • Infants with hyperkalaemia and abnormal ECG • Management of severe cardiotoxicity or cardiac arrest due to hyperkalaemia
Action	Insulin and glucose activate cellular sodium-potassium ATPase resulting in a potassium shift into the intracellular space.
Drug Type	Polypeptide hormone – lowers blood glucose and K^+.
Trade Name	Actrapid [Novo Nordisk] Humulin R [Eli Lilly] Hypurin Neutral Injection [Aspen]
Presentation	Vial: 100 units/mL in a 10 mL vial.
Dosage/Interval	**Treatment of hyperkalaemia with insulin—glucose 25% infusion** Starting dose: 0.1 unit/kg/hour. Dose range: 0.05 to 0.2 unit/kg/hour. Titrate infusion rate to serial serum potassium and blood glucose concentrations. **Treatment of hyperkalaemia with insulin-only infusion** Starting dose: 0.1 unit/kg/hour. Dose range: 0.05 to 0.2 unit/kg/hour. Titrate infusion rate to serial serum potassium and blood glucose concentrations. **Must have adequate maintenance fluids to prevent hypoglycaemia.** **Management of severe cardiotoxicity or cardiac arrest due to hyperkalaemia** 0.2 units/kg of insulin in glucose 50% IV over 15 to 30 minutes. **[Use this preparation if insufficient time to prepare insulin—glucose 25% infusion].**
Route	Intravenous
Preparation/Dilution	**Treatment of hyperkalaemia** **INSULIN—GLUCOSE 25% INFUSION – Run via central line**

Infusion strength	Prescribed amount
1 mL/kg/hour = 0.1 unit/kg/hour	5 units insulin and make up to 50 mL

Draw up 0.5 mL (50 units of insulin) and add 9.5 mL sodium chloride 0.9%, glucose 5% or glucose 10% to make a final volume of 10 mL with a concentration of 5 units/mL.
FURTHER DILUTE: Draw up 1 mL (5 units of insulin) of solution and dilute with glucose 25% [25 mL glucose 50% plus 24 mL water for injection] to make a final volume of 50 mL with a concentration/dose rate of **1 mL/kg/hour = 0.1 units/kg/hour.**

INSULIN ONLY INFUSION – Can be infused peripherally
Must have adequate maintenance fluids to prevent hypoglycaemia.

Infusion strength	Prescribed amount
1 mL/kg/hour = 0.2 unit/kg/hour	10 units insulin and make up to 50 mL

Draw up 0.5 mL (50 units of insulin) and add 9.5 mL sodium chloride 0.9%, glucose 5% or glucose 10% to make a final volume of 10 mL with a concentration of 5 units/mL.
FURTHER DILUTE: Draw up 2 mL (10 units of insulin) of solution and dilute with glucose 5%, glucose 10% or sodium chloride 0.9% to make a final volume of 50 mL with a concentration/dose rate of **1 mL/kg/hour = 0.2 units/kg/hour.**

Cardiac arrest due to hyperkalaemia

	<table><tr><th>Infusion strength</th><th>Prescribed amount</th></tr><tr><td>1 mL/kg/hour = 0.2 units/kg/hour</td><td>10 units insulin and make up to 50 mL</td></tr></table> Mix 25 g (50 mL of glucose 50%) glucose and 10 units regular insulin and give 1 mL/kg (0.2 units/kg of insulin) IV over 15 to 30 minutes. Glucose:insulin ratio = 2.5 g:1 unit.
Administration	**Intravenous:** Insulin is adsorbed to the plastic of intravenous bags, syringes and tubing which reduces the delivery of insulin.[1, 2] To saturate binding to plastic, infuse 20 mL of insulin solution through plastic tubing prior to infusion. Insulin concentrations ≤ 0.05 units/mL are not reliably delivered even after preconditioning and flushing [2]. Infuse with maintenance fluids. **Do not include in maintenance fluid requirements.** Insulin binds to the filter. Do not filter infusion.
Monitoring	Blood glucose must be closely monitored to detect either hypo/hyperglycaemia. Recommend blood glucose every 20 minutes for the first hour, every 30 minutes for the second hour and every 2 to 4 hours thereafter. Increase frequency of monitoring during weaning. Recommend check potassium within 30–60 minutes of commencing glucose/insulin infusion. Serum potassium should be closely monitored to monitor response to treatment and avoid hypokalaemia.
Contraindications	Hypersensitivity to human insulin or any component of the formulation. During episodes of hypoglycaemia.
Precautions	Possible adverse effects include hypersensitivity, hypoglycaemia, hyperglycaemia and hypokalaemia. Use with caution in cardiac disease, hepatic impairment, renal impairment.
Drug Interactions	The following may reduce insulin requirements: Octreotide, beta-adrenergic blocking agents, angiotensin converting enzyme inhibitors, salicylates, anabolic steroids, alpha-adrenergic blocking agents, quinine, quinidine and sulfonamides. The following may increase insulin requirements: Thiazides, furosemide, ethacrynic acid, glucocorticoids, thyroid hormones, sympathomimetics, growth hormone, diazoxide. Sympathomimetics have a potassium lowering effect.
Adverse Reactions	Insulin/glucose infusion is associated with a high rate of hyperglycaemia and hypoglycaemia during infusion and hypoglycaemia during weaning (insulin has a longer half-life than glucose). Hypokalaemia if infusion continued. Hypertonic solution – potential for extravasation.
Compatibility	Glucose 5%, glucose 10%, glucose 50%, sodium chloride 0.9%, lactated Ringer's injection **Y-site administration:** Azathioprine sodium; aztreonam; bretylium tosylate; bumetanide; buprenorphine hydrochloride; calcium chloride dihydrate; calcium gluconate monohydrate; caspofungin acetate; cefamandole nafate; cefazolin sodium; cefepime hydrochloride; cefotaxime; ceftazidime; ceftizoxime; ceftriaxone sodium; cefuroxime; chloramphenicol sodium succinate; cimetidine hydrochloride; clarithromycin; clindamycin phosphate; cyanocobalamin; dexamethasone sodium phosphate; doxapram hydrochloride; enalaprilat; epirubicin hydrochloride; epoetin alfa; erythromycin lactobionate; fentanyl citrate; fluconazole; folic acid (as sodium salt); foscarnet sodium; fosphenytoin sodium; ganciclovir sodium; hydrocortisone sodium succinate; ibuprofen lysine; imipenem-cilastatin sodium; indometacin sodium trihydrate; lidocaine hydrochloride; magnesium sulfate; mannitol; meropenem; methadone hydrochloride; methylprednisolone sodium succinate; metoclopramide hydrochloride; metoprolol tartrate; metronidazole; milrinone lactate; naloxone hydrochloride; netilmicin sulfate ; nitroglycerin; nitroprusside sodium; octreotide acetate; oxacillin sodium; pancuronium bromide; benzylpenicillin; phenobarbital sodium; phytomenadione; piperacillin sodium; potassium acetate; potassium chloride; procainamide hydrochloride; promethazine hydrochloride; propofol; pyridoxine hydrochloride; remifentanil hydrochloride; ritodrine hydrochloride; sodium bicarbonate; streptokinase; sufentanil citrate; tacrolimus; terbutaline sulfate; theophylline; thiamine hydrochloride; ticarcillin disodium; ticarcillin disodium-clavulanate potassium; urokinase; vancomycin hydrochloride; vecuronium bromide; verapamil hydrochloride; voriconazole

	In syringe: Insulin NPH.
Incompatibility	**Y-site administration:** Cefoxitin; chlorpromazine; diazepam; diazoxide; glycopyrronium bromide (glycopyrrolate); isoprenaline; ketamine; labetalol; micafungin; noradrenaline (norepinephrine); phentolamine; phenylephrine; phenytoin; piperacillin sodium-tazobactam sodium; polymyxin; propranolol; protamine; quinidine; rocuronium; sulfamethoxazole-trimethoprim;
Stability	Actrapid: Prepared solutions are stable at room temperature (< 25°C) for 24 hours. Humulin R: Prepared infusions can be stored refrigerated for 48 hours and may be used at room temperature for an additional 48 hours. A 20 mL insulin priming solution at a concentration of 0.1 units per mL was found to deliver 80% of the expected insulin [1]. A 20 mL insulin priming solution with additional preconditioning for 1 hour at a concentration of 0.05 units per mL was found to deliver 26.5% of the expected insulin [2].
Storage	Store human insulin preparations between 2 and 8°C. The shelf life is 30 months when stored between 2 and 8°C. Do not freeze. Human insulin preparations which have been frozen must not be used. Protect from excessive heat and light. Should appear clear and colourless. After first use, the vials may be kept at room temperature (below 25°C) for 4 weeks.
Special Comments	Recommend administer insulin/glucose in same line as intravenous fluids. Recommend intravenous fluids and/or an additional glucose 25% syringe placed proximally for rapid treatment of hypoglycaemia if needed. **Do not** include insulin in the total daily fluid intake. Frequent blood glucose and potassium estimations, especially after commencement and during weaning of infusion are needed for titration and safety.
Evidence summary	**Efficacy** **Treatment of hyperkalaemia:** A systematic review [3] of interventions for neonatal hyperkalaemia found 2 studies [4, 5] comparing insulin/glucose infusion versus rectal cation-resin. Meta-analysis of 2 studies (52 infants) found no difference in cardiac arrhythmias [RR 0.29; 95% CI 0.05, 1.65]; or all-cause mortality [RR 0.18; 0.03, 1.15]. Malone 1991, using an insulin infusion 0.05 to 0.2 units/kg/hour in albumin 5%, reported reduced treatment failure (rise in K^+ concentration > 0.5 mmol/L or K^+ > 7 mmol/L) of borderline statistical significance [RR 0.07; 0.00 to 1.01; RD -1.00; -1.28 to -0.72] compared to resin [5]. Hu 1999, using a glucose/insulin infusion with glucose 10–15 g:insulin 1 unit, reported a reduction in duration of hyperkalaemia [MD -12.20 hours; -20.95, -3.45]; no difference in peak serum K^+ [MD -0.10 mmol/L; -0.57, 0.37]; a reduction in IVH [RR 0.3; 0.10, 0.93] and IVH grades ≥ 2 [RR 0.3; 0.10, 0.93] compared to resin; and no infant with hypoglycaemia in either group [4]. No study compared insulin-glucose with a beta-agonist. **Conclusion:** The combination of insulin and glucose is preferred over treatment with rectal cation-resin for hyperkalaemia in preterm infants [3]. (LOE I GOR C) **Glucose:insulin ratio:** A historical control study compared infusions with lower glucose:insulin ratio 3.3 g:1 unit [glucose 20%] versus a higher glucose:insulin ratio 5 g:1 unit [glucose 30%] for treatment of hyperkalaemia and reported reduced rates of moderate hyperglycaemia [77% to 21.7% (p = 0.001)] with a single infant in the lower arm having hypoglycaemia [6]. (LOE III-3, GOR C). **Management of severe cardiotoxicity or cardiac arrest due to hyperkalaemia:** The Pediatric Advanced Life Support guidelines [7], Advanced Cardiac Life Support guidelines [8] and a simulation trial of medication preparation and delivery [9] support the following sequence of medications to treat hyperkalaemia during paediatric cardiac: First, calcium; second, sodium bicarbonate; and third, insulin with glucose. **Recommended dose [adult guideline]:** Glucose plus insulin: mix 25 g (50 mL of glucose 50%) glucose and 10 units regular insulin and give IV over 15 to 30 minutes. Glucose:insulin ratio = 2.5 g:1 unit. **Pharmacokinetics** Following IV administration, the observed half-life of insulin ranges from 5 to 15 minutes [Micromedex].
References	1. Thompson CD, Vital-Carona J, Faustino EV. The effect of tubing dwell time on insulin adsorption during intravenous insulin infusions. Diabetes Technol Ther. 2012;14:912-6.

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Original version Date: 29/05/2017	**Author: Neonatal Medicines Formulary Consensus Group**
Current Version number: 1.1	**Current Version Date: 12/08/2019**
Risk Rating: Low	**Due for Review: 12/08/2024**

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