Ballarat Health Services

DRUG GUIDELINE

Insulin, human neutral (Actrapid®) Intravenous Infusion for ICU, ED, Theatre and CVS

HIGH RISK MEDICATION

SCOPE (Area): **FOR USE IN:** Intensive Care Unit, ED, Theatre and CVS
EXCLUSIONS: Paediatrics (seek Paediatrician advice), Coronary Care Unit and General Wards
SCOPE (Staff): Medical, Nursing and Pharmacy

BRAND NAMES

Actrapid®.
Also known as neutral insulin, soluble insulin and regular insulin.
Insulin is available as many different forms. Only neutral human insulin (Actrapid®) is referred to in this guideline, and the use of the word insulin in this guideline refers to Actrapid® only.

PHARMACOLOGY AND PHARMACOKINETICS

Insulin increases or restores the ability to metabolise glucose by enhancing cellular glucose uptake, inhibiting endogenous glucose output and lipolysis. Insulin is almost completely metabolised (liver more than 50%, kidney 30%, remainder adipose and muscle tissue). The elimination half-life of Actrapid® insulin is 5-15 minutes after intravenous administration, as such the effect of insulin diminishes quickly once the infusion is ceased.
Actrapid® insulin excipients are glycerol, metacresol, zinc chloride (hydrochloric acid +/- sodium hydroxide is added to obtain a pH of 7.0 - 7.8).

INDICATIONS

- **For the treatment of hyperglycaemia and maintenance of glycaemic control in diabetics and non-diabetics (where required) in the Critical Care Areas.**

This guideline DOES NOT cover General Ward patients (See CPP0423 Diabetes – Insulin (actrapid) Glucose Infusion for Adults), Diabetic Ketoacidosis (see CPP0450 Management of Adult Diabetic Ketoacidosis), Hyperosmolar Non-Ketotic Syndrome, intrapartum patients (CPP0625 Insulin-glucose infusion during labour and birth) or the treatment of hyperkalaemia (see CPP0509 Hyperkalaemia Management) – seek Specialist advice.

CONTRAINDICATIONS

- Hypoglycaemia.
- Allergy to insulin or the excipients of Actrapid®.

PRECAUTIONS

- **Acute trauma or illness** – insulin requirements may increase.
- **Renal impairment** - less insulin may be required, however the monitoring of BGLs during the infusion will ensure the dose is adjusted appropriately. Dosing is unaffected by haemofiltration.
- **Hepatic impairment** – less insulin may be required, however the monitoring of BGLs during the infusion will ensure the dose is adjusted appropriately.

PREGNANCY AND BREASTFEEDING

Seek specialist advice before prescribing, information may update regularly.

DRUG INTERACTIONS

- **Betablockers** – may mask some hypoglycaemic warning symptoms and increase the incidence and severity of hypoglycaemia.
- **Corticosteroids, catecholamines -** may increase BGLs and increase insulin requirements.
- **Androgens, clarithromycin, disopyramide, fluoroquinolones, HIV protease inhibitors, hydroxychloroquine, lanreotide, MAOIs, octreotide, quinine, perhexiline, somatostatin, SSRIS, sulfamethoxazole, tramadol -** may decrease BGLs and decrease insulin requirements.
- **Drugs that lower potassium (e.g. diuretics), or are sensitive to the effects of low potassium (e.g. digoxin)** – insulin can cause/worsen hypokalaemia.

DOSAGE AND ADMINISTRATION

For administration only

- **in Intensive Care Unit, ED, Theatre and CVS**

Can be administered via CVC or peripherally. Do not administer on lines where other infusions may be bolused or flushes given.

Insulin is a high risk medication and MUST be independently double checked by two Registered Nurses or Medical staff.

Insulin infusions are NEVER to be run without a simultaneous and continuous caloric source (glucose 10% infusion, total parenteral nutrition or enteral feeding) in insulin dependent diabetics, except if the patient has severe hyperglycaemia (BGL greater than 30 mmol/L). A continuous caloric source must be also considered in non-insulin dependent or other patients requiring an insulin infusion. Any change in the rate of caloric source requires a review of the insulin infusion rate. Once the insulin infusion is ceased, the caloric source (if not ongoing) needs to continue for another 1-2 hours before ceasing. Subcutaneous insulin injection replacing the insulin infusion is to begin 30 minutes before the insulin infusion is turned off (usually in the morning or evening before a meal to facilitate transition to rapid acting and long acting insulin).

Insulin infusions are only safe and effective when monitored and adjusted. Observe for signs of hyperglycaemia and hypoglycaemia.

Type II diabetics may have insulin resistance and require higher rates of insulin infusion. When transferring back to oral antidiabetic agents in Type II diabetics typically lower than usual doses will be required, particularly if food intake has not returned to normal. It may be preferable to use a subcutaneous insulin sliding scale after ceasing the insulin infusion before recommencing oral agents. Cease any oral hypoglycaemics while administering an insulin infusion.

Insulin adsorbs onto glass, plastic, tubing and filters. The extent of this is difficult to establish and appears to vary with time. Monitor response to therapy and adjust the dose accordingly.

Consider the involvement of a Diabetes Educator.

Syringe Pump IV infusion (via CVC or peripheral vein):

Actrapid® insulin 50 units (0.5 mL) diluted to 50mL with sodium chloride 0.9% in a luer lock syringe for Alaris® pump with Syringe unit.

Total Volume: 50 mL.

Final concentration: 1 unit/mL.

Starting rate: As per Appendix 1 (Insulin (Actrapid®) IV infusion rates).

Rate increase: Adjust as per Appendix 1 (Insulin (Actrapid®) IV infusion rates) with a target BGL of 6.1-10 mmol/L unless otherwise documented by Registrar.

Usual rate range: 1-20 units/hr (1-20 mL/hr). Therapeutic dose varies between patients.

Ceasing infusion: Discuss ceasing infusion (and commencing subcutaneous insulin if appropriate) with the Registrar. When the insulin infusion is ceased the caloric source needs to be continued for another 1-2 hours. If transferring to subcutaneous insulin, give the first dose 30 minutes before the insulin infusion is turned off.

General Administration Information

- **Infusion preparation:**
  Mix infusion thoroughly (but gently) after adding Actrapid® insulin to avoid inadvertently giving a more concentrated dose.
  Other compatible infusion fluid may be substituted for sodium chloride 0.9% when deemed necessary by the Medical Officer.
  Infusion is stable for 24 hours.
- **Final concentration:** 1 unit/mL
- **Infusion Rate:** Variable
- **Infusion pump:** Alaris® pump with Syringe unit.
- **Routes of administration:**
  IV injection: Yes (not covered in this guideline)
  IV intermittent infusion: No
  IV continuous infusion: Yes
  IM injection: Only in an emergency under Medical guidance (not covered in this guideline)
  Subcut injection: Yes (not covered in this guideline)
- **Compatible/incompatible IV drugs/fluids:**
  Consult the Australian Injectable Drugs Handbook ('Yellow book') in your ward area. **Assume all unlisted drugs and IV fluids are incompatible – contact Pharmacy for further advice.**

MONITORING (INCLUDING BLOOD TESTS)

- BGLs should be reviewed by Medical staff regularly.
- Monitor potassium levels at least daily as insulin can cause hypokalaemia.

NURSING PRACTICE POINTS

- Check BGLs hourly for the first 4 hours, then if stable, 2 hourly or as directed by the Medical Staff. Less frequent readings are not recommended due to the risk of undetected hypoglycaemia. If commencing or ceasing parenteral or enteral feeding, check BGL hourly again for 4 hours.
- Monitor blood ketones for patients with insulin dependent diabetes (or other patients at risk e.g. acidotic) as per Blood Glucose Meters: Blood Ketone Monitoring Clinical Practice Protocol (CPP0439).
- Observe the patient for signs and symptoms of hypoglycaemia, hyperglycaemia and hypokalaemia.
- Monitor urine output.
- Monitor vital signs (including ECG) as indicated by the condition of the patient and Medical Staff.
- Regularly assess the conscious state of the patient (where able).
- Always prepare insulin infusions with two Division 1 Nurses.

- All Actrapid® solutions should be clear and colourless – visually inspect on drawing up.
- Label Actrapid® penfill with the patient's Bradma when using for the first time – ensure this is done in a way the name of the insulin can still be read. Also add the date the penfill was opened - the contents of the penfill are stable at room temperature (less than 25°C) for 28 days once removed from the refrigerator.
- Tissued infusions must be resited immediately.
- See Dosage and Administration section and Monitoring section for other information.

ADVERSE EFFECTS

- General - hypoglycaemia (see more information below), hypokalaemia (including cardiac arrhythmia), sodium retention and oedema, allergic reactions.
- **Hypoglycaemia** - the most frequent and serious adverse effect; may occur with excessive dosage, delayed or insufficient food, increased physical activity. Warning symptoms include sweating, hunger, faintness, palpitations, tremor, headache, visual disturbance and altered mood.

DRUG PRESENTATIONS, LOCATION AND STORAGE

Neutral human insulin (Actrapid®) 100 unit/mL 3mL penfills.
Refrigerate at 2-8°C, do not freeze. Contents of the penfill are stable at room temperature (less than 25°C) for 28 days once removed from the refrigerator. Protect from sunlight and excessive heat.

Appendix 1: INSULIN (ACTRAPID®) IV INFUSION RATES

FOR USE IN ICU, ED, THEATRE AND CVS ONLY

Note: The following is a guideline and cannot cover all circumstances or the variability of individual patient response. Vigilance, discussion and adaptation to individual requirements are essential. Consider the involvement of a Diabetes Educator.

AIM TO MAINTAIN BGL 6.1 – 10 mmol/L (or as advised by Medical Staff)

Insulin Dependent Diabetics

Start Actrapid® infusion at 1 unit/hr (1 mL/hr) plus caloric source. Actrapid® infusion is not to cease EXCEPT as outlined in the Ongoing Actrapid Infusion Rates table below (for BGL of 4 or under) OR 30 minutes after regular subcutaneous insulin has recommenced.

Non Insulin Dependent diabetics or others requiring insulin infusion

(BGL 10 or greater on two different occasions, two hours apart)

When commencing an Actrapid® infusion consider a caloric source.

Initial Actrapid® Infusion Rate

BGL (mmol/L)	Infusion rate (mL/hr = units/hr)
Less than 6	No infusion
6.1 – 10	1 mL/hr (insulin dependent only)
10.1 – 14	2 mL/hr
14.1 – 17	3 mL/hr
17.1 – 19.9	4 mL/hr
20 or greater	5 mL/hr (and contact Registrar)

- Check BGL hourly for 4 hours, then check BGL 2 hourly. Revert back to hourly BGLs for 4 hours if caloric source is altered.
- Glucose infusion (50mL/hr 10%) must be maintained unless enteral feeds are tolerated (i.e. 40 mL/hr or TPN started).
- Unstable patients with rapidly changing BGLs require hourly BGLs.

BGL (mmol/L)	Ongoing Actrapid® Infusion Rates (1 mL/hr = 1 unit/hr)
3.5 or less OR symptoms of severe hypoglycaemia (tremors, tachycardia, sweating, confusion, agitation, seizures, coma)	▪ Stop Actrapid® infusion ▪ Give glucose 50% 10-25 mL IV (peripheral line maximum 3 mL/minute) ▪ Check BGL in 15 mins ▪ When BGL 5 or more recommence infusion at half previous rate ▪ Review caloric source ▪ Contact Registrar
3.6 – 4	▪ Stop Actrapid® infusion ▪ Check BGL in 15 mins ▪ **When BGL 5 or more recommence** infusion at half previous rate ▪ Review caloric source
4.1 – 6	▪ If BGL decreased by 0.9 or less since last BGL, decrease infusion rate by 1 mL/hr ▪ If BGL decreased by 1 or more since last BGL, halve the infusion rate ▪ If BGL increasing, continue the current infusion rate
6.1 – 10 (target range)	▪ If BGL decreasing consistently and becomes 7 or less, decrease infusion rate to 75% of the current rate (to nearest half unit) ▪ Otherwise no change to rate
10.1 – 14	▪ If BGL decreased since last BGL, no rate change ▪ If BGL greater than or equal to last BGL, increase infusion rate by 1 mL/hr
14.1 – 17	▪ If BGL decreased by more than 2 since last BGL, continue same rate ▪ If BGL decreased by 2 or less since last BGL, increase infusion rate by 2 mL/hr ▪ If BGL increasing, increase infusion rate by 2.5 mL/hr ▪ If BGL not decreasing after two infusion rate increases, contact Registrar
17.1 or greater	▪ Test for ketones in urine and contact Registrar