Drug Guideline  
**Actrapid (neutral insulin)**

**Summary:**
Actrapid is a short acting human insulin preparation.

**Approved by:** ICU Medical Director

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**Next Review Date:** June 2016

**Replaces Existing Drug Guideline:** actrapid (neutral insulin), February 2002

**Previous Review Dates:** February 2002, October 2007.

**Background Information**

1,2: Actrapid lowers blood glucose levels by binding to insulin receptors to increase glucose uptake and inhibit hepatic glucose output.

Insulin is essential in the regulation of blood glucose, fat and protein metabolism. Intravenous insulin has a much more predictable action than subcutaneous insulin. Continuous intravenous insulin infusion is an appropriate means of controlling blood glucose levels during intensive care admission.

Once an insulin infusion has been commenced insulin needs time to diffuse into the body tissues before glucose transport is switched on. When insulin is given intravenously a small amount of glucose will start to disappear from the blood stream within a few minutes. However it will take another 2½ hours or more for the glucose uptake into the tissues to reach its maximum. Therefore, after the start of an insulin infusion, the blood glucose will be dropping much faster at 2 hours than it will be at 30 minutes. Because of this time delay in insulin working, the insulin infusion rate should not be changed more frequently than every 60mins.

In a similar way, insulin’s effects do not stop immediately after an insulin infusion is stopped. The blood glucose level may continue to drop for as long as 30 minutes or more after the intravenous infusion has been discontinued. This is because there is insulin still in the tissues that has to be broken down before it stops working. Hence it can be dangerous to stop the IV glucose at the same time as the insulin is stopped unless the patient is on enteral feeds or is about to eat.

1. **Introduction**, the risk addressed by this drug guideline:

   **Patient safety**

**The Aims / Expected Outcome of this drug guideline:**

Patients requiring intravenous (IV) insulin, will achieve and maintain a blood glucose level between 6.0-10.0mmol/L\(^3,4,8\). The patient’s level of hydration and plasma electrolytes will be monitored and maintained within normal limits.
**Related Policies**

- C3.00 Drug prescribing
- C3.01 Drug administration
- C3.01 Administration of IV Medications
- Diabetic Ketoacidosis
- Hyperosmolar hyperglycemic state

**2. Drug Guideline: Policy Statement**

- All care provided within Liverpool Hospital will be in accordance with infection control, manual handling and minimisation and management of aggression guidelines.
- Medications are to be prescribed and signed by a medical officer/authorised nurse practitioner (NP) unless required during an emergency.
- All drugs administered during an emergency (under the direction of a medical officer/authorised nurse practitioner) are to be documented during the event, then prescribed and signed following the event.
- Medications are to be given at the time prescribed (as close to the time as is possible when multiple drugs require ‘same time’ administration and, when the nurse is caring for more than one patient, recognition is given to a possible short delay to administration – antibiotics and other lifesaving drugs are to be prioritised) and are to be signed by the administering nurse.
- Parenteral medication prescriptions and the drug are to be checked with a second registered or endorsed enrolled nurse prior to administration. The “rights of drug administration” must be followed: right: patient, drug, dose, route, administration, time, reason for the drug, documentation, education and evaluation/outcome.
- Adverse drug reactions are to be documented and reported to a medical officer.
- Medication errors are to be reported using the hospital electronic reporting system: IIMS.
- Guidelines are for adult patients unless otherwise stated.
- Insulin infusions must be administered by syringe driver.
- When feeding is stopped, always obtain advice and a prescription, for a reduced insulin dose where appropriate or for additional IV glucose infusion.
- Patients who are on an Actrapid insulin infusion and who are to be transferred to a ward area must be referred to the endocrinology team and receive an appropriate diet/glucose infusion/insulin prescription according to the “Intravenous Insulin Infusion Orders” sheet (Form CR 132).

**3. Guideline**

**Actions**

Insulin is a pancreatic hormone, which is secreted from islets of Langerhans and Actrapid insulin is synthesized in-vitro by recombinant DNA technology

It decreases blood glucose levels by:
- Increasing the transport of glucose into cells.
- Inhibiting gluconeogenesis.
- Increasing glycogen formation or release.

It also:
- Stimulates protein synthesis.
- Increases the transport of potassium into cells.
- Lipogenesis

**Indications**

- Management of abnormal blood glucose level in Intensive Care patients. BGL is maintained between 6-10 mmol/L in ICU patients.
• Hyperglycaemia, BGL >10mmol/L
• Hyperkalaemia
• Significant elevated triglycerides

**Contraindications**
- Hypersensitivity to insulin.
- Hypoglycemia, BGL < 3mmol/L.

**Precautions**
- Monitor blood glucose levels especially during stress.
- Sepsis can increase patient’s insulin requirements.
- Drug therapy using beta-blockade (masks hypoglycaemic symptoms).

**Significant interactions**
- The following drugs may decrease with insulin requirements: monoamine oxidase inhibitors (MAOI’S), nonselective beta adrenergic blocking agents, angiotensin converting enzyme (ACE) inhibitors, salicylates, alcohol.
- The following drugs may increase insulin requirements: oral contraceptives, thiazides, frusemide, glucocorticoids, thyroid hormones, octreotide, growth hormone, diazoxide, nicotinic acid and inotropic agents such as adrenaline.
- Beta blocking agents may mask the symptoms of hypoglycaemia and delay recovery from hypoglycaemia.

**Adverse effects**
- Hypoglycaemia leading to unconsciousness
- If the BGL is lowered too fast in diabetic emergencies, it may lead to hypokalaemia and cerebral oedema.
- Hypersensitivity reactions can occur, must look for symptoms of redness swelling and itching.

**Presentation**
Actrapid human insulin, 100 units in 1 ml, 3 ml vial.

**Administrations Guidelines**

**Blood glucose level control within the intensive care unit to be maintained at 6-10mmol/L: (Please refer to Appendix 1 for Insulin Flow Chart).**
- Dilute 50 units actrapid to 50 ml sterile 0.9% sodium chloride in total to give a final concentration of 1 unit/ml.
- Commence at 1 to 2 unit/hour and increase by 0.5 to 1 unit/hour as necessary to maintain a BGL between 6-10mmol/L$^{3,4,8}$.
- Monitor blood glucose levels 2nd hourly until stable.
- If BGL is less than 15mmol/L insulin should run with IV glucose/ enteral / oral intake.
- When stable monitor BGL at 2-4 hour intervals
- If enteral feeds are ceased, closely observe BGL, titrate insulin and commence IV glucose.
- Cease infusion when BGL is less than 3-4 mmol/L.

**Hyperkalaemia**
- Give 50ml of 50% glucose as a slow IV bolus followed by 10 units actrapid insulin IV bolus.
- Perform ABG to carefully monitor BGL and potassium levels post management of hyperkalaemia.

**Diabetic Ketoacidosis$^{5,6,7}$ (Please refer to the ICU Guideline on Management of DKA)**
• Dilute 50 units Actrapid to 50 ml sterile 0.9% sodium chloride to give a concentration of 1 unit/ml.
• Confirm $K^+$ is > 3.3mmol/L
• Commence actrapid IV continuous infusion @ 0.1 units /kg/hr (usual starting rates may range from 4 to 10 units / hour). Aim for BGL reduction of 2 - 3 mmol/hr.
• If BGL does not drop by > 3mmol/hr in the first hour, double the rate of the infusion.
• If BGL drops by > 3 but < 6mmol/hr, continue actrapid infusion @0.1units /kg/hr.
• IF BGL drops by >6mmol /hr, seek medical advice. If the acidosis is resolving, may consider decreasing actrapid infusion to 0.05 units/kg/hr, if marked acidosis is still present this may not be ideal.
• When BGL <15mmol/L, reduce the actrapid infusion rate to 0.05 – 0.1units/kg/hr. DO NOT STOP INSULIN. If required give / increase glucose intake (persisting ketosis is a sign of inadequate glucose and insulin administration), e.g change to 10% glucose.
• Keep BGL between 8-11 mmol/L until DKA is resolved. (Resolution criteria – BSL <11mmol/L, Arterial pH > 7.3, HCO$_3^-$ > 18mmol /L).
• Once DKA has resolved if patient is nil by mouth continue intravenous insulin infusion and fluid replacement.

Hyperosmolar Hyperglycemic State (Please refer to the ICU Guideline on Management of HHS)$^5,6$

• Fluid replacement alone will result in a fall in BGL. Insulin treatment prior to adequate fluid replacement may result in cardiovascular collapse as water moves out of the intravascular space with resulting decrease in intravascular volume.
• Prepare Intravenous Actrapid infusion: Dilute 50units actrapid to 50mL sterile 0.9% Sodium Chloride, to give a concentration 1unit/mL.
• Low dose insulin 0.05 units/kg/hr should only be commenced once the BGL is no longer falling with IV fluids alone OR immediately if there is significant ketonaemia (3$\beta$ hydroxy butyrate >1mmol/L or urine ketones > 2+).
• The fall in BGL should be no more than 5mmol/L/hr. Measure hourly BGL.

Subcutaneous Insulin Therapy$^4,5$

• When the patient is able to eat, a multiple dose schedule should be started that uses a combination of short or rapid acting insulin and intermediate or long acting insulin. This should be done in consultation with the endocrinology team.
• There must be an overlap between the intravenous insulin infusion and the subcutaneous insulin dose. The intravenous insulin infusion should not be discontinued for at least 30-60 minutes after the administration of the subcutaneous dose. IV glucose administration should also continue for 60 minutes after the administration of the subcutaneous dose. This is critical for preventing worsened control and hyperglycemia.
• Estimating the Total Daily Dose (TDD) of insulin$^5$: this is based on patient’s sensitivity to insulin degree of glycemic control, insulin resistance, weight and age.

$$TDD = \text{Patients weight in kg} \times 0.5 \text{ to } 0.7 \text{units}$$

0.7 units is used for those thought to be more insulin resistant (teens, obese)

Eg: 72 kg patient TDD = 75 x 0.5 units = 36 units in 24hrs.

• The basal QDS regime for subcutaneous insulin: Give 50% of the TDD with the evening meal in the form of long acting insulin such as Lantus. Divide the remaining dose equally between pre-breakfast, pre-lunch and pre-evening meal in the form of rapid acting insulin.
Clinical Considerations

- Maintain BGL between 6-10mmol/L\textsuperscript{3,4,8}.
- Use separate vials (single patient use) for each patient to prevent contamination.
- Label vial with patient name and date of first use. Discard vial after 30 days usage. Transfer vial with patient when discharged from the Unit.
- Maintain refrigeration of vial after usage - when insulin actrapid is for intravenous use.
- Insulin that is for subcutaneous administration must not be kept in the refrigerator - label for individual patient use and keep at the bedside.
- Ensure adequate mixing of the vial contents (not shaken) prior to drawing-up.
- Test urine for glucose and ketones fourth hourly in all patients receiving actrapid insulin infusions and regular insulin regimens.
- When the BGL is < 10mmol/L, ensure there is a background glucose infusion (unless contraindicated) that may be used as a maintenance infusion - obtain fluid prescription.
- When feeding is stopped, always obtain advice and a prescription, for a reduced insulin dose where appropriate.

4. Performance Measures

All incidents are documented using the hospital electronic reporting system: IIMS and managed appropriately by the NUM and staff as directed.

5. References / Links


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Endorsed by: A/ Prof Michael Parr
APPENDIX 1: Infusion Flow Chart

Patients must have a glucose infusion or be fed

Measure blood glucose level on admission (known as 'BGL')
Normal range: 6 - 10 mmol/L

- **BGL > 10mmol/L**
  - Start insulin at 2 - 4 Units/hr

- **BGL 6 - 10mmol/L**
  - Start insulin at 1 - 2 Units/hr

- **BGL <6 mmol/L**
  - No insulin but check BSL every 4 hours

Measure BGL every 2 hours until in normal range:
> 6mmol/L and < 10 mmol/L

- **BGL > 10 mmol/L**
  - Increase insulin by 1 Unit/hour

- **BGL 6.0 to 10 mmol/L**
  - No change to the rate of the insulin infusion: BGL every 4 hours

- **BGL 4 - 6 mmol/L**
  - HALF the current insulin rate

- **BGL < 3 mmol/L**
  - STOP insulin, give 20mL of 50% glucose
    - Review with Medical Officer
    - Recheck BGL in 30 minutes

- **BGL 3- 4mmol/L**
  - STOP Insulin
    - Review with Medical Officer
    - Recheck BGL in 30 minutes