MIL

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This Medicines Information Leaflet is produced locally to encourage safe prescribing that is cost effective to the NHS. Information will be given on quality improvement issues and the costs to hospital and community.

Guidelines for Variable Rate Intravenous Insulin Infusions in Adults

This MIL provides guidance on the appropriate use of a variable rate intravenous (IV) insulin infusion (variable-RIII), previously known as "intravenous insulin sliding scale" for the management of blood glucose. Specialist settings are outside the scope of this MIL.

Do NOT use this guideline in patients with Diabetic Ketoacidosis (DKA), Hyperosmolar Hyperglycaemia state (HHS) or hyperkalaemia, see relevant MIL on the intranet.

Do not use this guideline where other approved specialist guidance exist e.g. stroke, maternity, transplant, Oxford Heart Centre.

Hyperglycaemia is a very common problem in hospital inpatients with diabetes and occurs in around 25%.[2] Patient outcomes are improved with good glycaemic control. Correcting in-hospital hyperglycaemia is current good clinical practice. Where tight glycaemic control is appropriate, target capillary blood glucose (CBG) is 6-10 mmol/L, but readings in the range 4-12 mmol/L are acceptable[1,2]. Use of variable-RIII typically achieves this target by infusing a constant rate of glucose-containing IV fluid while infusing insulin at a variable rate. It is important to note that for some patient groups tight glycaemic control is not appropriate (e.g. end of life, frail elderly). In these cases the prescriber must specify the target CBG range within the Variable-RIII prescription.

Patients **without** known diabetes who present or develop hyperglycaemia during an acute illness (undiagnosed /stress hyperglycaemia) have much higher in-hospital mortality. This patient group needs to be managed in exactly the same way as those with known diabetes.[2]

Indications for Variable-RIII

Ward- based medical inpatients

1. Hyperglycaemia (glucose over 12 mmol/L) with recurrent vomiting (unless DKA/HHS– follow relevant MIL)
2. Hyperglycaemia in the context of severe illness including sepsis
3. Nil by mouth [NBM] (**missing two or more meals**)
   a. Procedures (if insulin treated)
   b. Prolonged starvation e.g. unsafe swallow (although prolonged use of Variable-RIII is unlikely to be appropriate)

Ward-based surgical inpatients

1. All patients with diabetes treated with insulin who are likely to miss two or more meals for elective or emergency procedures
2. All patients with type 2 diabetes who miss two or more meals, remain NBM and develop persistent hyperglycaemia (CBG over 12 mmol/L for more than 2 hours)
3. Patients with HbA1c over 69 mmol/mol (8.5%) in whom surgery cannot be delayed
4. All patients presenting with acute severe pancreatitis and persistent hyperglycaemia (CBG more than 12 mmol/L)

Starting a variable-RIII

Ensure the patient has **dedicated** IV access for variable-RIII

Prescription

In ePMA use the 'Insulin Variable Rate Infusion Power Plan'.

Insulin - Adult Variable Rate Infusion PowerPlan

See Appendix for guidance on how to access this within ePMA.

Long-acting insulin analogues (Abasaglar®, Lantus®, Levemir®, Toujeo®, Tresiba®) should continue to be **prescribed and given** in the patient's usual dose and times alongside insulin infusion.
If these long-acting analogues have been inadvertently stopped please restart.
Withhold all other diabetes medicines while on variable-RIII (prescribe then suspend these in EPR)

Select the appropriate insulin infusion regimen
Indicate which regimen to follow (see table).

For patients new to insulin: start with standard regimen

For patients already on insulin treatment the starting regimen depends on the usual total daily insulin dose. Add up all the regular subcutaneous (SC) insulin in a 24 hour period.

If 24 hour SC insulin requirement is:

- less than 30 units start on **reduced** regimen
- between 30 and 99 units start on **standard** regimen
- 100 units or more start on **increased** regimen

The PowerPlan may need to be accessed on more than one occasion to ensure accurate prescription of insulin and IV fluid.

The initial insulin infusion rate should be determined by the bedside CBG measurement according to the table below.

Blood Glucose (mmol/L)	**Insulin Infusion Rate** (units/hr)			
	Standard Regimen (first choice in most patients)	**Increased Regimen** (for insulin resistant patients)	**Reduced Regimen** (for insulin sensitive patients)	**Tailored Regimen** (according to individual patient need)
0 – 3.9	Withhold insulin infusion and treat hypoglycaemia according to MIL			
4 - 6	0.5	0.5	0.5	
6.1 - 8	1	2	0.5	
8.1 -12	2	4	1	
12.1 - 16	4	6	2	
16.1 - 20	5	7	3	
Over 20 *__NB__. check infusion running & line patent	6	8	4	

Before increasing insulin infusion rate for hyperglycaemia the following must be checked: cannula is patent, tubing and infusion equipment are working appropriately, insulin and glucose co-infusions are running at the correct rate.

CBG should be checked hourly.

If **CBG less than 4 mmol/L (hypoglycemia)**:

1. Stop infusion and treat for low blood glucose according to the hypoglycaemia MIL
2. **Recheck CBG 15 minutes later**:
   - If 4mmol/L or above restart insulin infusion as per CBG.
   - If remains less than 4 mmol/L, repeat hypoglycaemia treatment until CBG is 4 mmol/L or above, then step down to lower regimen (e.g. intensive to standard). If already on reduced regimen seek specialist diabetes advice following hypoglycaemia treatment.
   - IV insulin must be restarted within 20 minutes of CBG being above 4 mmol/L.

If **CBG over 12 mmol/L, then** check capillary ketones.

- If ketones less than 1 mmol/L recheck in CBG in 1 hour and continue to check ketones if CBG remains over 12 mmol/L.
- If ketones between 1-3 mmol/L, risk of Diabetic Ketoacidosis (DKA), recheck ketones in 1 hour. If still elevated then step up to increased regimen. But also re-check after 2 hours if last ketone was 1-3 mmol/l even if CBG has fallen below 12 mmol/L.
- If ketones above 3 mmol/L, check venous bicarbonate or pH, change to DKA MIL if needed. If not DKA then step up to increased regimen and re-check ketones in 1 hour.

Adjusting infusion regimen to achieve target CBG

If CBG remains *over 12 mmol/L for 3 consecutive hourly* readings **and** is *not dropping by 3 mmol/L per hour or more*, recheck the result, and if the result is confirmed, move to the next higher regimen (e.g. reduced to standard, standard to increased). If already on increased regimen prescribe a tailored regimen.

CBG too tight

If CBG is between 4-6 mmol/L on two or more consecutive hourly readings consider reducing to a lower regimen in those patient groups where this is undesirable e.g. acute coronary syndrome.

Administration

- Use human soluble insulin 1 unit/mL pre-filled syringe 50 mL [unlicensed medicine] (available from pharmacy or emergency drug cupboard and stored in ward fridge).
- Administer insulin and glucose containing infusion via a single cannula via a Y-connector with dual anti-reflux valves (NHS code FKA322) and a syringe pump extension set with integral anti-syphon valve (NHS code FKA040) to connect to the insulin. *[Alternatively, two lumens of central line is acceptable but anti-syphon and one-way valve protection is required for each solution].*
- IV insulin must be administered via a syringe pump.
- Two registered professionals must set up and check initial insulin infusion rate and for each rate change. This is recorded by both signing the prescription for administration.
- If the insulin and/or glucose infusion are disconnected from the patient, new solutions and new giving sets should be used.

Monitoring

Measure and record CBG hourly (day and night); adjust infusion rates accordingly. This is vital to ensure the prompt treatment of hypoglycaemia (patients may be unaware or too ill to alert staff; drowsiness may be wrongly attributed to sedation). It also minimises the risk of uncontrolled hyperglycaemia and prompts a review of the infusion equipment and insulin rate.

Avoiding hypoglycaemia

Ensure the patient receives a suitable glucose source to prevent hypoglycaemia. This must never be discontinued, especially during transfer.

In most patients this is as a constant rate glucose containing IV infusion. This can be adequately provided by diet, enteral feed, parenteral nutrition or in a dialysate. However, review need for Variable-RIII in patients on enteral feed or diet, and consider referral to the Inpatient Diabetes Specialist Team.

Intravenous Fluid and Electrolyte Management

Take the underlying medical condition into account when determining the choice of fluid and the infusion rate.

- Glucose containing IV infusion must be administered via a volumetric pump.

Intravenous insulin causes hypokalaemia, by shifting potassium from the intravascular to the intracellular space. Hypokalaemia is a potentially serious complication of intravenous insulin therapy. Therefore monitor serum potassium concentration at least daily and aim to maintain it in the reference range (3.5–5 mmol/L).

The rate of fluid replacement should be set in line with the fluid requirements of the individual patient. If in doubt seek advice from a Registrar or Consultant.

The preferred fluid for administration alongside variable-RIII is 4% glucose & 0.18% sodium chloride with potassium 20 mmol per litre (0.15%) to run at 100 mL/hr, rate adjusted according to clinical requirements.
If serum potassium outside target range (3.5-5 mmol/L) adjust as below:

Serum potassium (mmol/L)	Potassium replacement (mmol or iv fluid/%)
less than 3.5	40 mmol per L (0.3%)
3.5-5	20 mmol per L (0.15%)
above 5	Nil

For patients in whom **fluid overload is a concern** use 10% glucose with potassium 10 mmol (0.15%) in 500mL to run at 50mL/hr, rate adjusted according to clinical requirements. If serum potassium outside target range (3.5-5 mmol/L) adjust as below:

Serum potassium (mmol/L)	Potassium replacement (mmol or iv fluid/%)
less than 3.5	20 mmol per 500ml (0.3%)
3.5-5	10 mmol per 500ml (0.15%)
above 5	Nil

Patients on dialysis – discuss IV fluid regimen with Renal Consultant or Specialist Registrar, do not give potassium unless serum potassium is less than 3.5mmol/L.

Avoiding hyponatraemia

Ensure daily sodium requirements are met to prevent hyponatraemia and check electrolytes daily.
Additional fluid therapy may be required according to the specific needs of the patient for a given surgical procedure.

The following patients are likely to need fluid containing sodium chloride to avoid hyponatraemia:

- Variable-RIII for more than 24 hours and
- Vomiting, pyrexial or dehydrated

This is usually in the form of sodium chloride 0.9% (via a second infusion line). In those patients in **whom fluid overload is a concern** sodium chloride 0.9% with glucose 5% is available in a 500mL bag with or without 10 or 20 mmol potassium chloride [unlicensed medicine] as an alternative. When prescribed this can be sourced from pharmacy (including out of hours).

Essential measures for the safe maintenance of a variable-RIII:

- *Hourly monitoring of CBG*
- *Regular review of insulin infusion rate to achieve target range of glucose*
- *At least daily review of the need for the Variable-RIII*
- *At least daily clinical review of patient including fluid status*
- *Daily urea and electrolytes (more frequent if unstable)*
- *If patient is hyponatraemic or potassium less than 3 mmol/L seek advice from Medical or Anaesthetic Consultant or Specialist Registrar*

Refer patients where variable-RIII continues for more than 48 hours to the diabetes team (see contact details).

Transition from Variable-RIII to Subcutaneous Insulin

- The switch from IV to SC meal-time insulin should be delayed until the patient is able to eat and drink normally, without nausea or vomiting. This should happen preferably at breakfast, but no later than 5pm.
- Make sure the SC insulin is available to be administered.
- Patients on a previously established insulin regimen should be restarted. Doses may have to be adjusted, depending on the patient's clinical condition or if reduced caloric intake.
- Continue IV insulin infusion for one hour after the SC insulin has been administered to allow time for the insulin to be absorbed. After discontinuation of variable-RIII monitor CBG 2 hourly for first 6 hours, then every 4-6 hours for the first 24 hours.
- Patients who have not previously used SC insulin – seek expert advice.
- Other diabetes medication should be restarted, if still appropriate, when patient is eating and drinking normally. Stop variable-RIII one hour after the first dose is administered.

Common pitfalls:

- Do not alternate glucose fluids with 0.9% sodium chloride 0.9% according to CBG.
- Do not prepare insulin infusions in the clinical area instead of getting a pre-filled syringe (safety concerns).
- Do not use variable rate *subcutaneous* insulin infusions for acute hyperglycaemic emergencies, e.g. DKA, HHS.
- Do not use glucose potassium insulin (GKI) infusions e.g. Digami.
- Do not omit long-acting insulin analogues (Abasaglar®, Lantus®, Levemir®, Toujeo®, Tresiba®).

Inpatient Diabetes Nursing Team Contacts (Oxford and Horton sites):
Tel: 01865 (2)22866 – leave message out of hours
E-mail: diabetessupportnurses@ouh.nhs.uk or,
adultinpatient.diabetesteam@nhs.net
(All referral much be sent by e-mail)

For advice (bleep)**:** JR 4433/4103/6138, CH 6762, NOC 6761, HGH 9912
For urgent out of hours review or advice please contact the on-call Diabetes SpR via OUH Switchboard

References:

1. Joint British Diabetes Societies for inpatient care (JBDS-IP). The use of variable rate intravenous insulin infusion (VRIII) in medical inpatients. October 2014. Available at http://www.diabetologists-abcd.org.uk/JBDS/JBDS.htm
2. JBDS-IP. Management of adults with diabetes undergoing surgery and elective procedures: Improving standards. September 2015.
3. Rickard et al., Slipping up on the sliding scale: fluid and electrolyte management in variable rate intravenous insulin infusions. Prac Diabetes 2016;33

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Summary of Variable Rate Intravenous Insulin Infusion in Adult MIL

Recognise Need

Medical Inpatients	Surgical Inpatients	Refer to specialist guidance in:

• **Capillary Blood Glucose (CBG) above 12 mmol/L** plus:
  • Severe illness or sepsis
  • Recurrent vomiting
• **Nil by mouth** (missing two or more meals) plus:
  • Insulin treated & awaiting procedure
  • Prolonged starvation
	• **Nil by mouth** (missing two or more meals) plus:
	  • Insulin treated & awaiting surgery
	  • CBG above 12 mmol/L for 2 hours
	• **HbA1c greater than 69 mmol/mol (8.5%)** and surgery cannot be delayed
	• **Acute severe pancreatitis** and CBG persistently above 12 mmol/L
		• Intensive Care
		• Oxford Heart Centre
		• Maternity
		• Stroke
		• Transplant
		• Under 18s

NOT FOR USE IN DIABETIC KETOACIDOSIS (DKA) OR HYPERGLYCAEMIC HYPEROSMOLAR STATE (HHS)

Prescribe Insulin

1. **Continue** long-acting subcutaneous insulin
   Including Lantus®, Levemir®, Abasaglar®, Toujeo®, and Tresiba®
2. **Suspend** all other subcutaneous insulin and other diabetes medication
3. **Prescribe continuous intravenous insulin infusion** according to patient's normal total daily insulin usage:

Total daily insulin 30 - 99 units (or new to insulin)	Total daily insulin 100 units or more	Total daily insulin less than 30 units
Prescribe STANDARD REGIMEN	Prescribe INCREASED REGIMEN	Prescribe REDUCED REGIMEN

Prescribe Glucose

1. **Prescribe rescue glucose infusion**
   (75 mL of 20% intravenous glucose PRN for hypoglycaemia)
2. **Prescribe glucose-containing intravenous fluid for ALL patients** according to fluid and electrolyte status:
   (unless glucose requirements can be fully met with enteral / parenteral nutrition or dialysate)

HyPOvolaemic / Euvolaemic

K^+ less than 3.5	100 mL/hr of 4% Glu + 0.18% NaCl with 40 mmol K^+ per Litre
K^+ 3.5 - 5	100 mL/hr of 4% Glu + 0.18% NaCl with 20 mmol K^+ per Litre
K^+ greater than 5	100 mL/hr of 4% Glu + 0.18% NaCl

Prescribe separate 0.9% Sodium Chloride infusion according to fluid and/or Na^+ requirements

HyPERvolaemic / Fluid restricted

	Na^+ less than 135	**Na^+ 135 or more**
K^+ less than 3.5	50 mL/hr of 0.9% NaCl + 5% Glu with 20 mmol K^+ per 500 mL	50 mL/hr of 10% Glu with 20 mmol K^+ per 500 mL
K^+ 3.5 - 5	50 mL/hr of 0.9% NaCl + 5% Glu with 10 mmol K^+ per 500 mL	50 mL/hr of 10% Glu with 10 mmol K^+ per 500 mL
K^+ greater than 5	50 mL/hr of 0.9% NaCl + 5% Glu	50 mL/hr of 10% Glu

Setup

1. **Infuse IV insulin through syringe pump:**
   ALWAYS use human soluble insulin 1 unit/mL pre-filled syringe 50mL and a syringe pump extension set with integral anti-syphon valve (NHS code FKA040)
2. **Infuse IV glucose-containing fluid through volumetric pump:**
   Insulin and glucose infusions MUST both be connected to a single site of IV access via Y-connector with dual anti-reflux valves (NHS code FKA322), or two lumens of a central line with one-way and anti-syphon valves
3. **All other medications and infusions must be given through a separate IV access device**

Titration & Monitoring

1. **Commence insulin infusion according to initial capillary blood glucose (CBG)** as per table below
2. **Measure CBG hourly throughout day and night** plus measure ketones if indicated below
3. **Titrate insulin infusion according to CBG:**

Blood Glucose (mmol/L)	Insulin Infusion Rate (units/hr)			
	STANDARD Regimen	INCREASED Regimen	REDUCED Regimen	
0 - 3.9	Withhold insulin infusion and treat hypoglycaemia - recheck CBG after 15 mins			**CBG 4 mmol/L or more:** restart insulin within 20 mins **CBG less than 4 mmol/L:** repeat hypoglycaemia treatment until CBG above 4 mmol/L then restart insulin on next lower regimen within 20 mins
4 - 6	0.5	0.5	0.5	Consider reducing to next lower regimen in high risk patients (i.e. acute coronary syndrome) if CBG 4 - 6 for two consecutive readings
6.1 - 8	1	2	0.5	
8.1 - 12	2	4	1	
12.1 - 16	4	6	2	**Check cannula and lines patent + infusions running** **Check ketones:** if 1 -3 mmol/L patient risk of DKA - • recheck ketones in 1 hr and increase to next higher regimen if ketones still elevated. • (if next CBG in range recheck ketones in 2 hrs) **If ketones above 3 mmol/L:** take venous blood gas and request Doctor to review - switch to DKA protocol if indicated, or increase to next higher regimen and recheck in 1hr if DKA protocol not indicated **If three consecutive CBG readings above 12 mmol/L** and not dropping by 3 mmol/L per hour**:** increase to next higher regimen and recheck in 1 hr
16.1 - 20	5	7	3	
Above 20	6	8	4	

Seek advice from Diabetes SpR / Consultant and prescribe tailored regimen if CBG persistently low on Reduced Regimen or if CBG persistently high on Increased Regimen

4. **Prescribe new IV glucose infusion after each bag completed:** NEVER give IV insulin without glucose
5. **Check Urea and Electrolytes daily** and adapt fluid prescription to maintain normal Na^+ and K^+
6. **Review need for Variable Rate Insulin Infusion daily** and discontinue when appropriate

Refer all patients on Variable Rate Insulin Infusions for 48 hours or more to Inpatient Diabetes Team

Ending Variable Rate Infusion

1. **Switch to subcutaneous insulin when:**
   - The patient is able to eat and drink normally
   - No further nausea and vomiting
   - Subcutaneous meal-time insulin available for administration
2. **Switch should ideally take place at breakfast** and always before 5pm - do not switch overnight
3. **Restart subcutaneous meal-time insulin at previously established dose(s)**
   Doses may need to be adjusted according to clinical condition and/or calorific intake
4. **Seek specialist advice for patients not previously using subcutaneous insulin**

Give patient meal → **Administer sub-cutaneous Insulin** → **Continue IV insulin for 1 hour then stop** → **Measure CBG 2 hrly for first 6 hrs** → **Take CBG 4 - 6 hrly for first 24 hrs**

For patients on other diabetes medications only

Restart diabetes medications once eating and drinking normally (if still appropriate) and stop IV insulin at time of first prescribed dose