Northern Care Alliance
NHS Foundation Trust

Management of Hyperglycaemia and Hypoglycaemia in Critical Care (QRG)

Lead Author and contact details	Dr Rhodri Harris Consultant in Intensive Care Medicine & Anaesthesia Rhodri.harris@nca.nhs.uk
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What is new in this version	This document is a revised version of the Salford Care Organisation "Critical Care Blood Glucose Guidelines (2018)" and a new guideline for Oldham and Bury. It contains updates on: • Revised glucose targets. • HbA1c. • Updated QRG's for all short & long-acting insulins and non-insulin medications. • Guideline on the use of Fixed Rate Insulin Infusions in critical care.
Keywords	ICU, CCU, Glucose, Hyperglycaemia, Hypoglycaemia

Hyperglycaemia Protocol in Critical Care

(Diabetic Ketoacidosis /Hyperosmotic emergencies—use Trust Protocols)

ESTABLISH DIAGNOSIS

All admissions should have HbA1c and laboratory or ABG/VBG glucose checked
Glucose should be checked every 6 hours in the critically ill patient, daily when more stable

Known diagnosis of diabetes

Review and prescribe usual medications as appropriate (see QRG)

HbA1c >60mmol/mol
Poor control, at greater risk of complications from IV insulin such as hypoglycaemia

Request non urgent DSN review

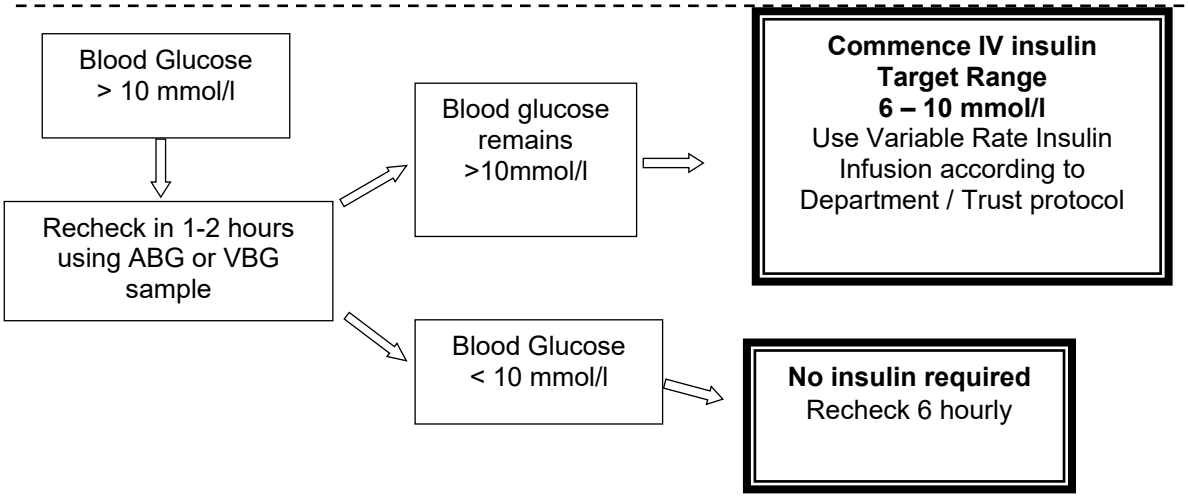
No previous diagnosis of diabetes

HbA1c > 48mmol/mol
New diagnosis of diabetes
(Type 1 / Type 2 / gestational)
Request DSN review

HbA1c < 48mmol/mol
Critical illness (Stress) Hyperglycaemia
Steroid Induced Hyperglycaemia
(Does not exclude Diabetes)

Accuracy of Glucose Measurements
Laboratory sample = ABG or VBG on gas analyser > Arterial blood on POC >>Capillary (finger prick) POC**
**Accuracy in capillary samples is worse at extremes of measurement in critically ill patients.
(any unexpected low or high sample should be double checked with another sample from a different source)

COMMENCE TREATMENT



DAILY REVIEW

Hypoglycaemia	Review episodes, assess and document risk factors and adjust medication and nutrition to minimise repeat episodes
IV Insulin	Calculate total insulin requirements last 24 hours. Consider adding other medication if diabetic (metformin/long-acting insulin) > 48 units in 24 hours = high risk
Glucose Checks	Is glucose being checked frequently enough? Ensure bead head sign and discuss barriers to sampling and high risk medications at handovers
HbA1c	Was HbA1c checked on admission? Discuss and document diabetes diagnosis in notes. Refer to DSN if > 60mmol/mol
Long-acting Insulin	Review daily (see separate QRG). Consider titration according to daily insulin requirement. Check availability of long-acting with nurse/pharmacist.
Oral & other diabetes medications	Can usual medications be restarted? Review daily (see separate QRG).

Hypoglycaemia Protocol in Critical Care

AVOIDANCE

Looming Hypoglycaemia
Blood glucose < 6.0 mmol/l on an insulin infusion?
STOP INSULIN INFUSION
Recheck in 30 minutes and 1 hour

Risk Factors
1. Not checking blood glucose frequently enough
IV insulin—every hour
Subcutaneous insulin—every 4 hours
2. Interruptions in nutrition
Feed breaks/displaced NGT/fasting for procedures or scans. Ensure IV glucose as an alternative and stop IV insulin if no nutrition
3. Medication change (check long-acting insulins)
4. Resolving critical illness & drug excretion

TREATMENT

Blood Glucose < 4.0 mmol/l
Four is the Floor—Treat Immediately
STOP INSULIN INFUSION!

Recheck blood glucose at 15, 30 and 60 minutes or until >4.0mmol/l

Does the patient have a central line?
Yes → **50ml of 50% glucose via CVC line over 10 minutes (followed immediately by 0.9% NaCl flush**

No

Does the patient have a peripheral cannula?
Yes → **250ml of 10% glucose via a peripheral cannula over 15 minutes**

No

Is there an enteral route?
Yes → **200ml orange juice or 6 glucose tablets PO or crushed down NG + 1mg Glucagon IM**

No → **2 tubes of Glucogel via gums + 1mg Glucagon IM**

LEARNING

Hypoglycaemia is a risk in ICU patients, take steps to improve future management
- Document the episode: include details of insulin, oral medications, nutrition etc
- Review risk factors to avoid a further episode
- Discuss on next Handover & Ward Round— review insulin treatment

Episode of hypoglycaemia (<4.0mmol/l) in a critical care patient: complete Incident form. Regular audit of hypoglycaemia episodes

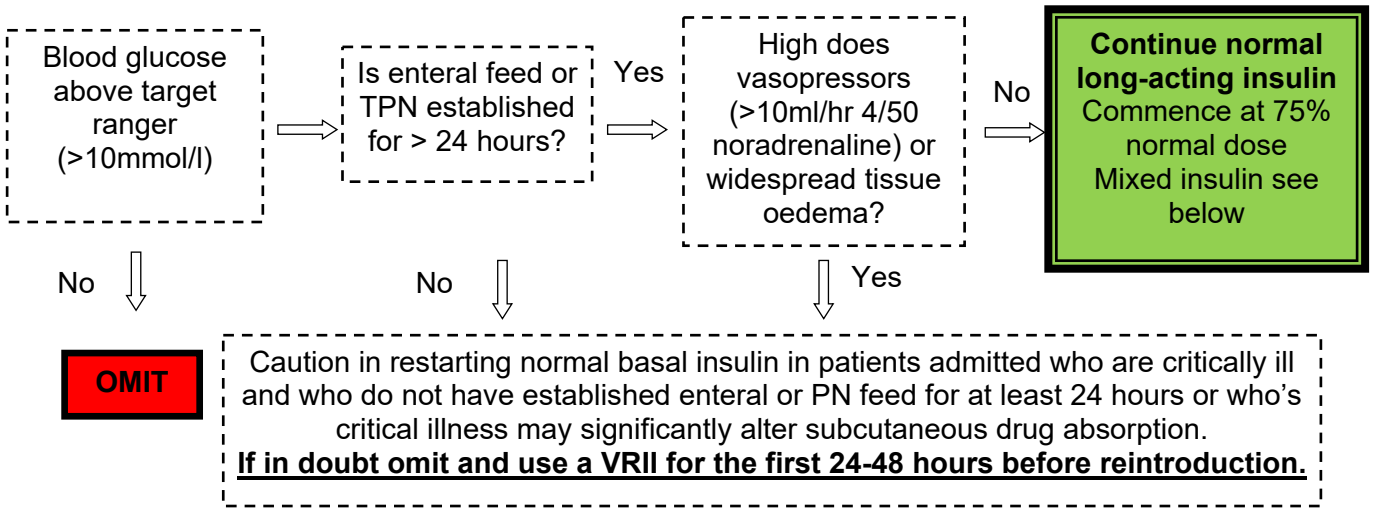
Long-acting (basal) Insulins

Long acting insulins are used in persons with diabetes to replace or in addition to background insulin release by the pancreas. They be given once or twice daily via subcutaneous injection.
Examples: Lantus, Toujeo & Abasalgar (insulin glargine), Levemir (insulin detemir), Tresiba (insulin degludec), Insulatard / Humilin I (Isophane insulin)

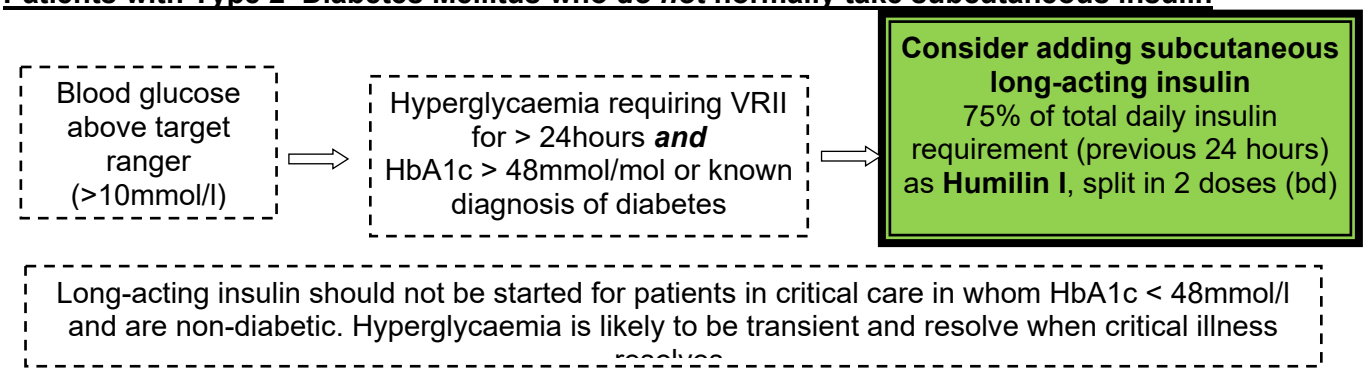
Patients with Type 1 Diabetes Mellitus who normally take subcutaneous insulin

Do not omit long-acting insulin in patients with Type 1 Diabetes Prescribe patient's usual dose and ensure appropriate background nutrition.

Patients with Type 2 Diabetes Mellitus who normally take subcutaneous



Patients with Type 2 Diabetes Mellitus who *do not* normally take subcutaneous insulin



Long-acting insulin should not be started for patients in critical care in whom HbA1c < 48mmol/l and are non-diabetic. Hyperglycaemia is likely to be transient and resolve when critical illness resolves

Blood glucose target range in critical care is 6.0 –10.0mmol/l. However on subcutaneous insulin and when critical illness is resolving, this target range may be increased to 6.0 –12.0mmol/l in line with ward guidelines. This change should be clearly documented in the Diabetes Management Plan.
Subcutaneous absorption is affected by vasopressors, oedema, shock, hypothermia, pyrexia. Long-acting insulin should be administered subcutaneously in tissue least affected by oedema and localised scarring or lipohypertrophy. The area with best absorption is assumed to be the abdomen but in cases where marked dependent oedema occurs, the upper arm may be preferable.
Dose adjustments should be 20% at most every 48-72 hours (seek advice from Diabetes Specialist Nurse).
Basal Insulin should be started with caution in Steroid Induced Hyperglycaemia, particularly in short courses of steroids. Contact Diabetes team if starting for medium or long term courses and before discharge from Critical Care.
Mixed insulin—prescribe 75% of total 24-hour dose as long-acting insulin (Levemir) split into 2 doses 12 hourly.

Patient normally takes:		First line (if immediately available)	Second line (if not immediately available)
Basal / long-acting insulins			
Insulin type	**Brand name**		
Insulin Glargine	Lantus	Usual insulin	Lantus (same dose) at 10pm
Insulin Glargine	Toujeo	Usual insulin	Lantus (same dose) at 10pm
Insulin Glargine	Abasalgar	Usual insulin	Lantus (same dose) at 10pm
Insulin Detemir	Levemir	Usual insulin	Lantus (same dose)
Insulin Degludec	Tresiba	Usual insulin	Levemir (same dose split bd)
Isophane Insulin	Humilin I	Usual insulin	Insulatard (same dose usual time)
Isophane Insulin	Insulatard	Usual insulin	Humilin I (same dose usual time)
Rapid / short-acting insulins			
Insulin Aspart	Fiasp	Usual insulin	Novorapid or Actrapid (same dose)
Insulin Aspart	Novorapid	Usual insulin	Novorapid or Actrapid (same dose)
Insulin Aspart	Trurapi	Usual insulin	Novorapid or Actrapid (same dose)
Insulin Glulusine	Apidra	Usual insulin	Novorapid or Actrapid (same dose)
Insulin Lispro	Humalog	Usual insulin	Novorapid or Actrapid (same dose)
Insulin Lispro	Sanofi	Usual insulin	Novorapid or Actrapid (same dose)
Insulin Lispro	Lyumjev	Usual insulin	Novorapid or Actrapid (same dose)

- **Mixed / Combination insulins** (e.g., Humulin M3)
  These preparations contain both short or rapid acting insulin plus an intermediate acting insulin in a fixed ratio (Humulin M3 = 30% short-acting, 70% long-acting)
  The unpredictable tissue absorption and switch from normal diet means that these are of increased risk in critically ill patients.
  If a patient normally takes a mixed insulin and is admitted to ICU, in general their mixed insulin should be converted to a long-acting insulin to avoid boluses of short acting insulin.

To convert mixed insulin to long acting insulin only use 75% of the total dose of mixed insulin usually taken over 24 hours into a twice daily dose of a long-acting insulin.

For example: patient normally takes Humulin M3 24 units morning and 16 units evening.

Prescribe: Long-acting insulin @ 75% of total daily dose divided 12 hourly

= [(24+16) x 0.75] / 2

= 15 units of Levemir 12 hourly (bd)

Metformin
Biguanides. An oral medication that decreases hepatic glucose production and increases peripheral glucose uptake without risk of hypoglycaemia.

Patients with Type 2 Diabetes Mellitus who normally take metformin

- No enteral route / surgical contraindication to enteral medications
- Shock requiring > 10ml/hr (4mg/50ml) noradrenaline or equivalent
- Acute or chronic liver failure
- Acute kidney injury (AKI) Stage 2 or 3 (increase serum creatinine >200%, urine output < 0.5ml/kg/hr for >12hours or on renal replacement therapy)
- Lactic Acidosis (Lactate >2mmol/L)

No ⇨ **Continue metformin** Liquid preparation for NG use (not modified release)

Yes ⇨ **OMIT**

Patients with Type 2 Diabetes Mellitus who do not normally take metformin OR new diagnosis of diabetes with blood glucose > 10mmol/l)

Hyperglycaemia (>10mmol/l) requiring IV insulin in last 24 hours ⇨ Type 2 Diabetes Mellitus diagnosis OR HbA1c > 48mmol/mol on this admission ⇨ Check contraindications above ⇨ **Consider starting metformin 500mg bd**

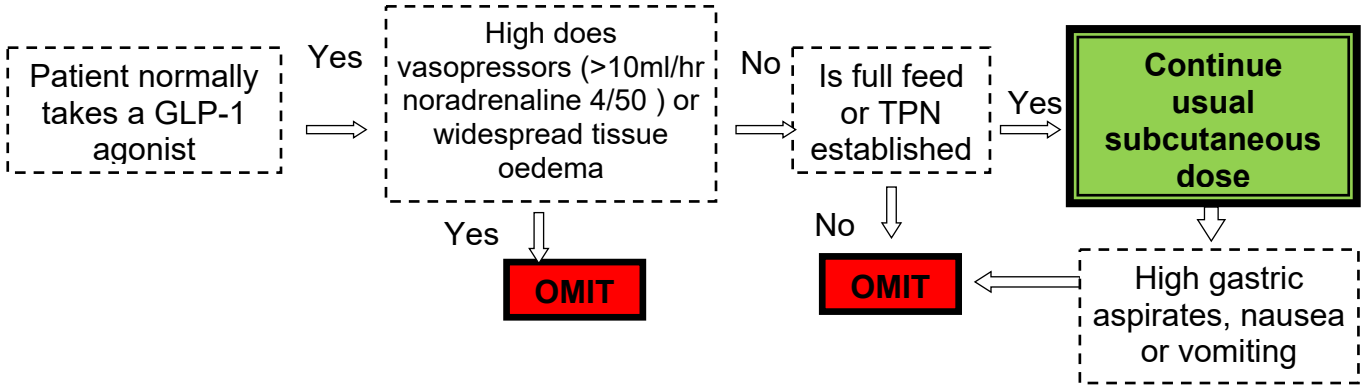
May be associated with a lactic acidosis in patients with shock, renal impairment or in liver injury, omit in these circumstances.

Unlikely to be a cause of hypoglycaemia. May reduce the need for intravenous insulin and therefore decrease glucose variability.

Early reintroduction may be beneficial in critically ill patients already taking metformin. If enteral feed is established and no surgical contraindications consider restarting early

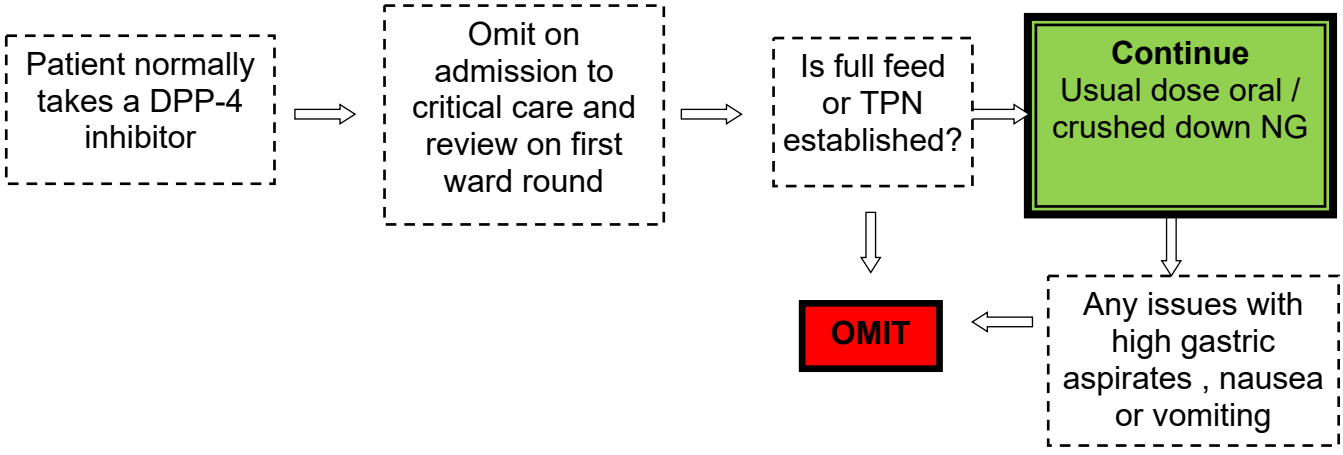
Monitor lactate—if rising above 2mmol/l omit metformin.
Metformin is excreted unchanged in the kidney and can accumulate rapidly in Acute Kidney Injury, it's use in critical care should be reviewed daily.

<u>Glucagon-like peptide-1 (GLP-1) agonists:</u> Exenatide/Liraglutide/Semaglutide
Subcutaneous injection. Incretin mimetic, blocks glucagon release, increases insulin release to glucose and slow gastric emptying



Exanatide,Lirgalutide and other GLP-1 agonists cause delayed gastric emptying (and therefore reduce postprandial hyperglycaemia). This may cause problems with absorbing NG feed. Should be stopped in patients with high GI aspirates.
The risk of hypoglycaemia is low. GLP-1 agonists have been demonstrated to be an effective agent in controlling blood glucose in critically ill patients at high doses, but their use at high doses was limited by gastrointestinal side effects. In the absence of high gastric aspirates or nausea these agents can be safely continued in patients who are already using them .
Continuing usual diabetes medications reduces the need for IV insulin and improves glycaemic variability

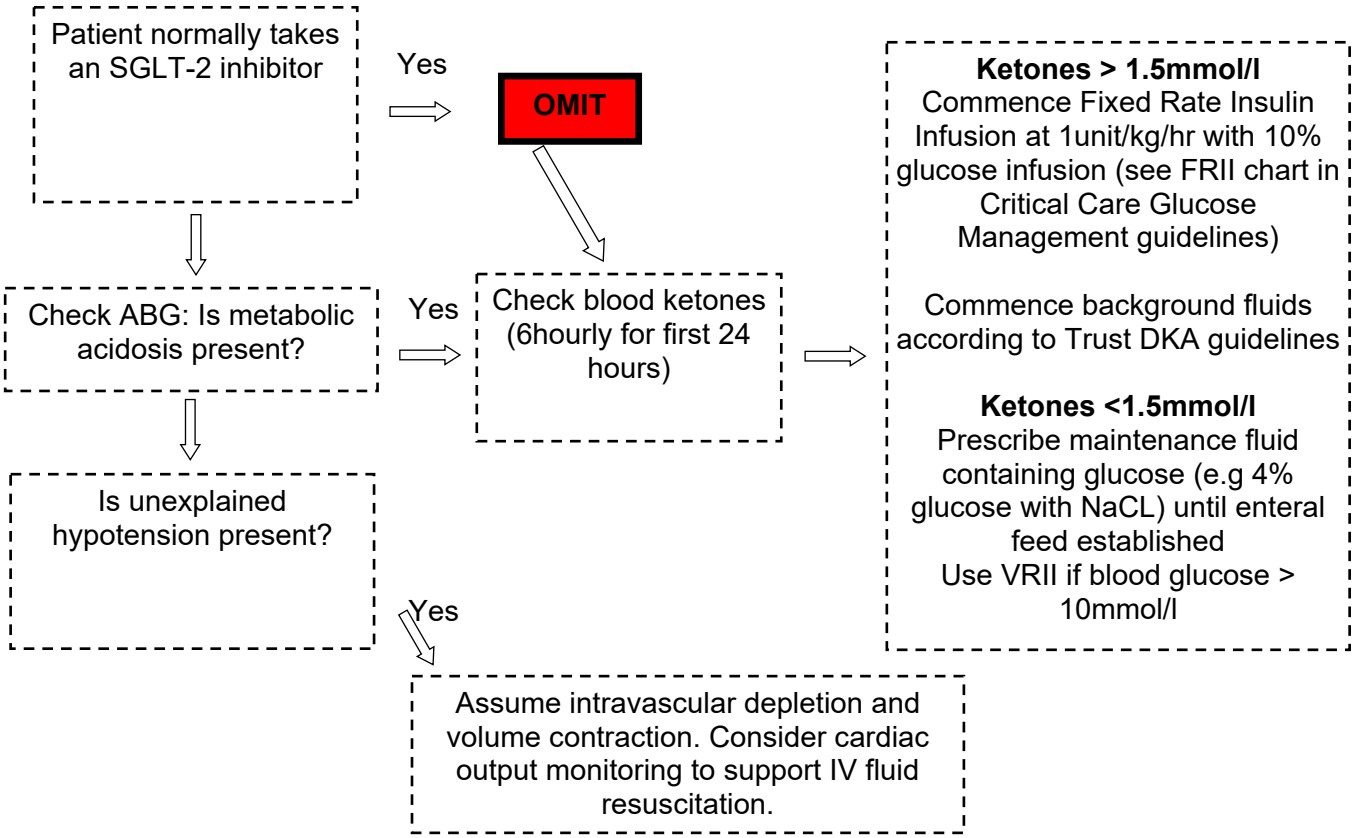
<u>Dipeptidyl peptidase-4 (DPP-4) inhibitors:</u> Sitagliptin / Linagliptin
Oral medication with a similar mechanism to the GLP-1 agonists. Increase incretin levels therefore suppress glucagon release, increases insulin release to glucose and slow gastric emptying.



May be associated with GI disturbance, nausea, vomiting
Rare reports of pancreatitis

Less risk of hypoglycaemia than other antidiabetic agents

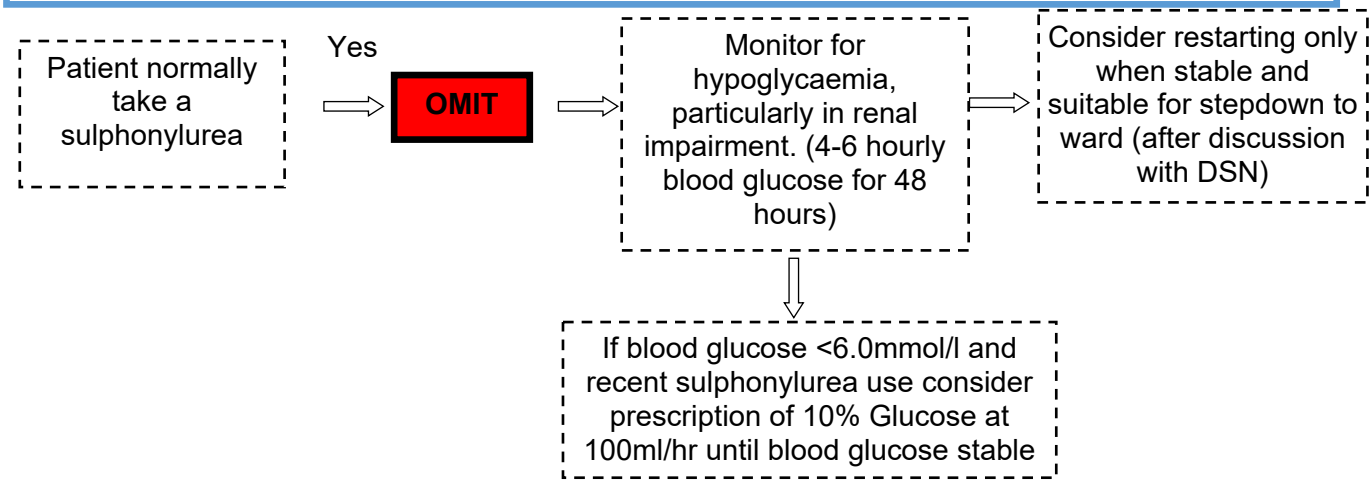
Sodium-glucose co-transporter-2 (SGLT-2) inhibitors:
Canagliflozin, Dapagliflozin & Empagliflozin
Reversibly inhibit sodium-glucose co-transporter 2 in the renal proximal convoluted tubule to reduce glucose reabsorption and increase urinary glucose excretion. Indicated for use in Type 2 diabetes and congestive cardiac failure.



SGLT-2 inhibitors are associated with a risk euglycemic ketoacidosis that may exist for several days after discontinuation of treatment. This is a particular risk to critically ill patients and those patients that have a sudden reduction in calorie intake (e.g vomiting secondary to gastroenteritis). Unexplained acidosis in a patient admitted who has been taking a SGLT-2 inhibitor should prompt investigation for ketoacidosis even in the context of normal glucose levels.

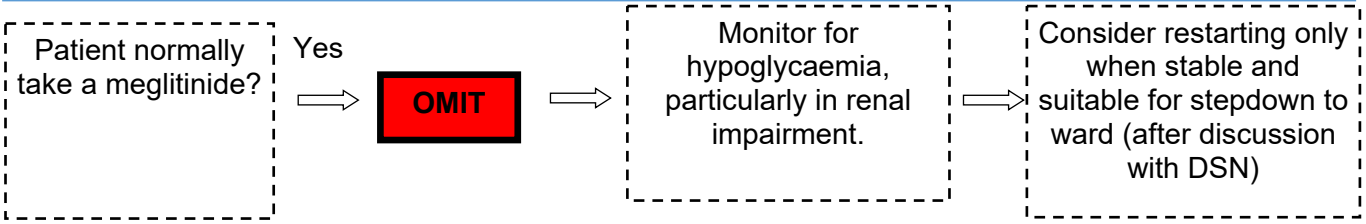
Patients should have their SGLT-2 inhibitors held for a minimum of 72 hours preoperatively. If continued before surgery then ensure nutrition (glucose maintenance containing fluid)

<u>Sulphonylureas:</u> Gliclazide/ Glimepiride
bind to receptors on Beta cells causing increased release of insulin



High risk for hypoglycaemia in critically ill patients and in those with drug accumulation in renal failure.
Multiple drug interactions
There may be a role for using gliclazides in Critical Care patients who are weaning from critical illness. They may aid in reducing the need for a VRII, basal insulin and decrease glucose variability.
Gliclazide is indicated as first line management in SCO guidelines for steroid induced hyperglycaemia. In critically ill patients they are less likely to be effective in this situation and IV insulin may be preferable.
They should only be started/continued after discussion with the Diabetes Specialist Nurse.

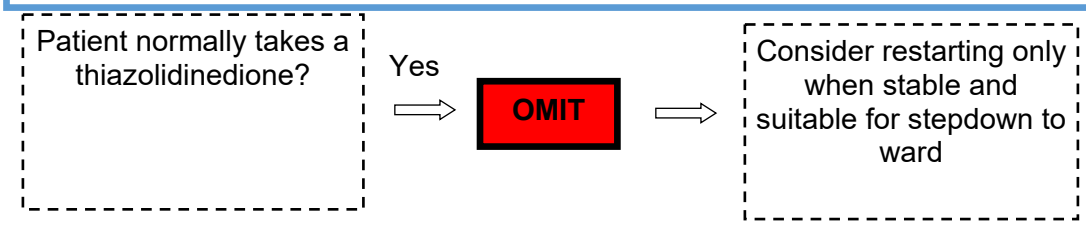
<u>Meglitinides:</u> Repaglinide/ Nateglinide / Metiglinide
bind to receptors on Beta cells causing increased release of insulin



Shorter acting and less potent than sulphonylureas but may still cause significant hypoglycaemia.
There may be a role for using meglitinides in Critical Care patients who are weaning from critical illness.They may aid in reducing the need for a VRII, basal insulin and decrease glucose variability.
They should only be started/continued after discussion with the Diabetes Specialist Nurse.

Thiazolidinediones: Pioglitazone

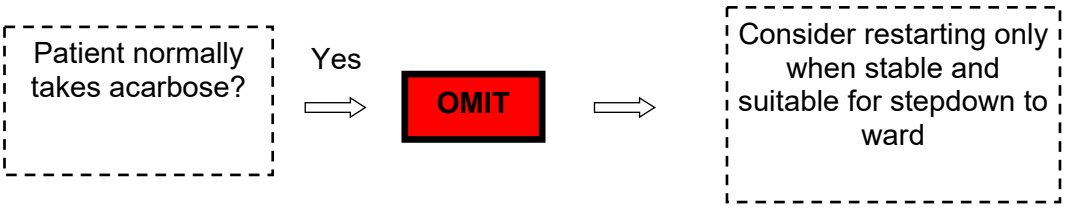
Bind to nuclear receptors increasing uptake of free fatty acids into adipocytes resulting in increased glucose metabolism



Can cause fluid retention, peripheral oedema and worsen congestive cardiac failure.
Pharmacological actions are via nuclear binding receptors so hypoglycaemia can occur in fasting patients many days after stopping therapy.
Should be discontinued whilst in critical care

Alpha-glucosidase inhibitors: Acarbose

Intestinal brush border enzyme inhibitor



Likely to cause GI disturbance and diarrhoea.
Omit whilst on critical care