



# Management of Hyperglycaemia in Adult Critical Care

*AIM: To provide guidance for the safe use of IV insulin (Variable Rate Insulin Infusion, VRII) for the control of blood sugars in in the critically ill patient, diabetic and non-diabetic, to maintain normoglycaemia*

## Key Points

This guideline covers the management of the hyperglycaemic patients in the adult critical care unit.

It is based on the NICE-SUGAR study which included diabetic patients type-1 and type-2 and non-diabetic patients with hyperglycaemia during their admission to critical care, which require intravenous administration of a Variable Rate Insulin Infusion (VRII).

The management of diabetic emergencies such as Diabetic Ketoacidosis and Hyperosmolar Hyperglycaemic State, are covered on a separate guideline.

## Insulin Infusion Guideline

### Indications for starting a variable rate insulin infusion:

1. **Hyperglycaemia** in patients not normally on insulin (more than 2 consecutive blood glucose levels (BGLs) of >10 mmol/L)
2. Insulin dependent diabetics who cannot maintain regular enteral carbohydrate intake and/or cannot take subcutaneous insulin

### Principles of monitoring:

- Check **BGLs** hourly for two hours, then 2-hourly for 4 hours if acceptable (i.e., within target range or trending towards target range). Once **BGLs** are stable and within range, switch to 4-hourly monitoring.
- If 7 out of 10 readings are out of range, consider protocol individualisation of target **BGLs**
- Check **BGLs** in 1 hour after any changes to glucose/nutrition intake or insulin infusion rate

### Before starting a variable rate insulin infusion:

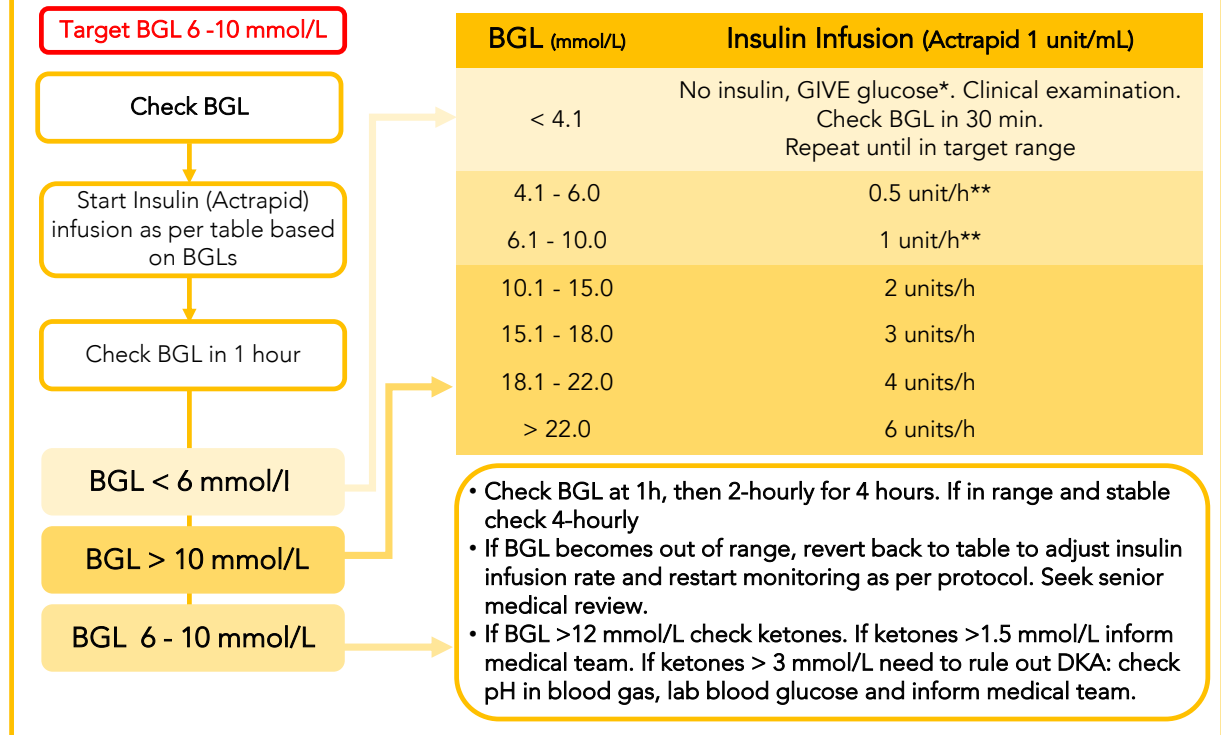
- Consider indication for starting
- Decide which protocol to follow: **DIABETIC INSULIN-DEPENDENT** or **NON-DIABETIC / DIABETIC NON-INSULIN-DEPENDENT**
- Ideally use BGL from an arterial blood gas.
- Note the potassium level.
- Ensure that an IV source of glucose ± potassium is running at all times while patient on VRII, unless patient eating well.
- Ensure prescription and administration of insulin is correct.

### To be aware of during infusion:

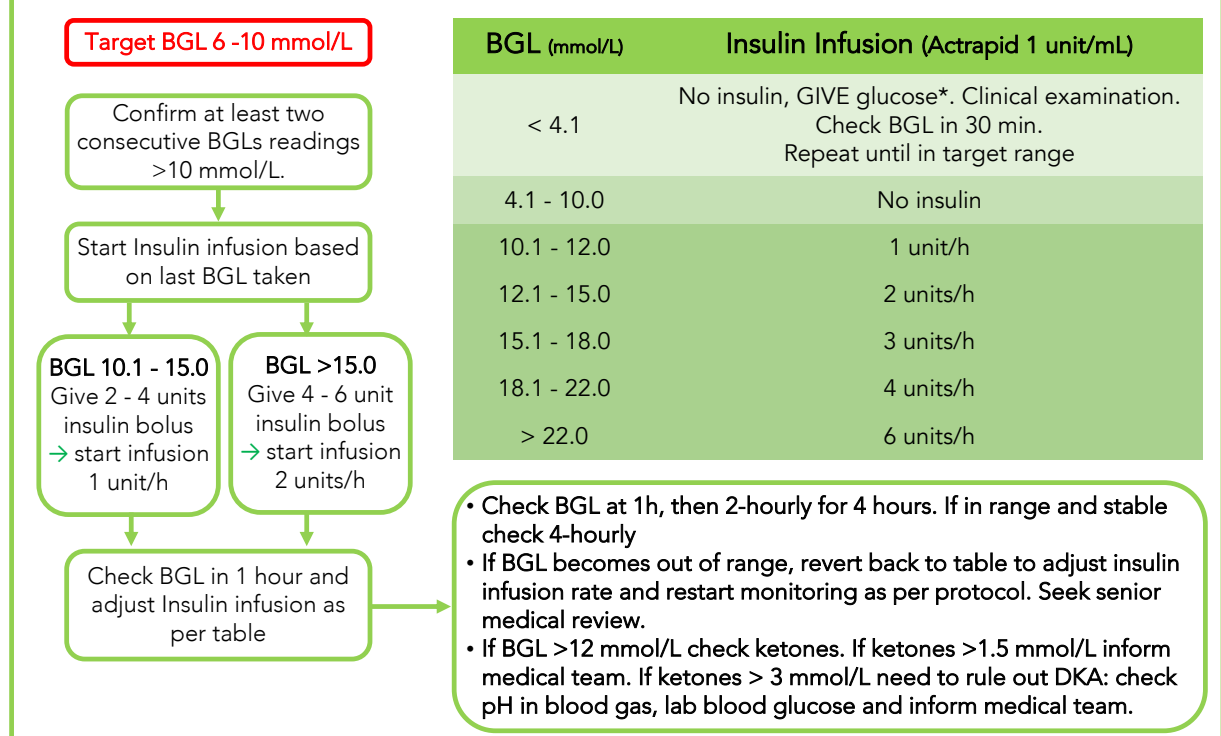
1. **Monitor Potassium (K<sup>+</sup>) Level**  
Administration of insulin reduces K levels. Check K<sup>+</sup> on ABG specimen at least **twice daily** or more often if insulin rate high or changing.
2. **Notify medical team** if any of the following:
  - **Prior to cessation** of feed or glucose infusions. Medical team to consider decreasing or ceasing the insulin infusion.
  - Insulin infusion running at **≥ 8 units/hour**. Take another blood sample from another site and **send to the laboratory**
  - **K<sup>+</sup> <3.5**
3. **Changes to feeding regimes and rest periods.** Be aware that Actrapid insulin has an onset period of 30 minutes to 1 hour which may cause rapid changes in **BGLs**. Increase **BGLs** monitoring to hourly until stable again.



### Hyperglycaemia on Insulin Dependent Diabetic Patients



### Hyperglycaemia on Non-Diabetic and Non-Insulin Dependent Diabetic Patients



**Note if patient has a change of nutrition or glucose intake, increase BGL monitoring to hourly until stable again**

\*If BGL <4.1 give Glucose 10-20% 50-100 mL over 30 min and recheck BGL  
\*\*In Type 1 diabetic patient (IDDM) ensure basal insulin is running at all times



## Introduction

Elevated blood glucose in critically ill patients is a common clinical finding and is associated with increased mortality and poor outcomes. The aetiology of hyperglycaemia in critical illness is multi-factorial and occurs in both diabetic and non-diabetic patients. Endogenous cytokines and hormones such as cortisol and adrenaline reduce insulin production and increase insulin resistance, promoting glycogenolysis and gluconeogenesis whilst impairing peripheral utilisation. Many of the critical care therapies such as exogenous steroids and catecholamine's further exacerbate the situation. However, the results of the NICE-SUGAR study in 2009 indicate that tight glucose control with intravenous insulin results in worse outcomes than moderate control due to increased tendency to develop hypoglycaemia.

## Definitions

<b>BGL</b>	Blood Glucose Level
<b>BM</b>	Boehringer Mannheim test: A blood glucose measurement performed on a glucose meter
<b>IDDM</b>	Insulin Dependent Diabetes Mellitus
<b>NIDDM</b>	Non-insulin Dependent Diabetes Mellitus
<b>DKA</b>	Diabetic Ketoacidosis
<b>HHS</b>	Hyperosmolar Hyperglycaemic State
<b>HONK</b>	Hyperosmolar Non-Ketosis – old fashioned term for HHS
<b>VRII</b>	Variable Rate Intravenous Insulin Infusion
<b>GLP-1 analogues</b>	Glucagon-like peptide-1 analogues. Anti-diabetic medicines which are subcutaneously injected but are NOT insulin. Examples include Exenatide (Byetta & Bydureon) and Liraglutide (Victoza). Not to be confused with Insulin.

## Duties and responsibilities

Implementation of this guideline is the joint responsibility of appropriate critical care medical/nursing staff. This guideline is subject to professional judgement and accountability.



# Process

## INCLUSION CRITERIA

Action	Rationale
All adult patients admitted to critical care requiring variable rate intravenous insulin infusion	The protocol used in this guideline is based on the NICE-SUGAR study which included type 1, type 2 and non-diabetic patients with hyperglycaemia admitted to critical care.

## EXCLUSION CRITERIA

Action	Rationale
DKA / HHS	The management of DKA / HHS requires fixed rate intravenous insulin infusion with potentially large volumes of fluid delivered and close attention to the rate of decline in serum glucose. The DKA protocol should be followed for these patients.
Paediatric patients	The NICE-SUGAR protocol was not validated in children whose insulin sensitivity and fluid requirements are significantly different to that of an adult.

## USE OF GUIDANCE

Action	Rationale
Stratify patients onto correct protocol depending on whether they are insulin dependent or non-insulin dependent diabetics.	Patients with <b>Type 2</b> and <b>non-diabetic</b> will retain some residual insulin producing pancreatic function. <b>Type 1</b> diabetics have no endogenous insulin secretion and so require a basal level of insulin even within range to inhibit ketogenesis. Therefore, it is necessary to have a protocol for each patient.
Prescribing clinician to indicate which regimen the nurse is to follow	It is mandatory that the VRII prescriptions indicate which regime is to be followed
Continue patients regular long-acting insulins particularly in type 1 diabetics once the patient is in the convalescent phase of their illness or time on IV insulin infusion is likely to be short	Hyperglycaemia and DKA have been reported in type 1 diabetics who have VRII discontinued without long-acting agent already on board. IV insulin has a very short half-life and effects will dissipate in a matter of minutes when the infusion is stopped. Physiologically a healthy pancreas produces a continuous background level of insulin to suppress ketogenesis. Type 1 diabetics will not produce sufficient background insulin when stopping the insulin infusion and are at risk of DKA. Keeping the long-acting insulin on board from beginning of the VRII ensures a smooth and safe continuity when the VRII is stopped.



Action	Rationale
<p>Ensure a source of glucose is prescribed and is run alongside the insulin infusion. Acceptable sources of glucose are:</p> <ul style="list-style-type: none"> <li>- Glucose 4%/NaCl 0.18%</li> <li>- Glucose 10% - 20% - 50%</li> <li>- Enteral feed</li> <li>- Parental feed</li> </ul>	<p>Incidents have occurred where patients have had IV insulin without a source of glucose and have developed hypoglycaemia.</p> <p>Always run a source of glucose to oppose the insulin to prevent this.</p> <p>The National Diabetes Association guidelines state that critical care units are permitted to use a wider range of glucose sources than are permitted for lower dependency wards including enteral feeds which are not acceptable on the wards.</p>
<p>The bedside nurse should run the insulin infusion at a rate determined by BGL</p>	<p>The protocols used were validated in the NICE-SUGAR trial in critically ill patients as a means of attaining adequate control of BGLs.</p>
<p>Blood sugars should be monitored either via BM monitoring or from blood gas analysis. Monitoring must be hourly initially for 2 hours, reducing to 2 hourly for 4 hours then 4 hourly if BM's remain in target range. Increase frequency of monitoring if BM's move persistently out of range (&gt; 2 reading of &gt;10 mmol/L despite adjustment of the rate)</p> <p><b>Target range 6 - 10 mmol/L</b> (unless specified by a consultant)</p>	<p>The frequency of monitoring is as per the NICE-SUGAR protocol. Intensive blood glucose control was associated with a higher mortality than conventional blood glucose control. Excessive finger-prick testing is unpleasant for patients and excessive arterial blood sampling can contribute to anaemia.</p> <p>A range of 6 -10 mmol/L is sufficient in most patients to reduce harmful effects of hyperglycaemia in critical illness without chasing a range that is too tight and results in hypoglycaemia.</p>
<p>The clinician should review the prescription every 24 hours and adjust if necessary to attain &gt; 70% blood glucose readings within target range</p>	<p>Patients have variable insulin sensitivities and for some the standard algorithm may have too little or too much effect. For example, obese patients, those in septic shock or those receiving corticosteroids may have up to 4 x the requirement. Whereas renal patients often have much lower insulin requirements. Prescribers should therefore tailor the guideline rates to the patient's specific insulin sensitivity. For assistance in how to individualise, speak to duty consultant or pharmacist.</p>
<p>Ensure in the absence of hyperkalaemia that adequate potassium is included with IV fluids in all patient on IV insulin. Closely monitor K<sup>+</sup> and correct abnormalities as they occur.</p>	<p>Insulin induces the movement of potassium ions into the cells via action at the insulin receptor. Inadequate supplementation of potassium with an insulin infusion can precipitate hypokalaemia.</p>



## DISCONTINUING INSULIN INFUSION

Action	Rationale
In non-insulin dependent patients the IV insulin can be discontinued when patient has been on 0mls/hr for 48hours	Blood sugars remaining in normal range without IV insulin for a protracted period in such patients suggest the driver for their hyperglycaemia has resolved and the insulin is no longer required
For Type 1 diabetics the IV infusion should be discontinued around a mealtime. Give the usual dose of their short acting insulin prior to meal (30 mins for short acting, 15 mins for rapid acting). 15 mins after finishing meal, switch off IV insulin.	Mealtime is the safest time to discontinue IV insulin in type 1 diabetics as this allows a short-acting insulin to be given, in conjunction with food to mimic normal physiological profile of endogenous insulin
Check BM's 1 hour after stopping insulin infusion in type 1 diabetes	This ensures there is not rebound hyperglycaemia upon cessation of IV insulin.
Patients who have required insulin due to TPN-induced hyperglycaemia can be transitioned to subcutaneous insulin by prescribing total daily dose of IV insulin (once stable) as Insulatard/Humulin I. Give 50% of calculated dose and stop the infusion 30 minutes later. Give the other 50% after 12 hours.	This is the most efficient regime for controlling BM's in patients on continuous parenteral nutrition. Regimes calculating short-acting insulins are ineffective since the IV administration of glucose is continuous whilst long-acting insulins pose greater risk of hypoglycaemia and are difficult to titrate
Patients normally on continuous subcutaneous insulin pumps at home should have input from diabetes team prior to IV insulin being discontinued	Such patients are a specialist population with the pump technology not being in the remit of expertise of critical care staff

## STARTING SUB-CUTANEOUS INSULIN IN PREVIOUSLY NON-INSULIN PATIENTS

Refer to the Diabetes Team in the first instance

<p>Weight based calculation Frail, elderly, hepatic failure, CKD stage 4/5 or newly diagnosed Type 1 diabetes <b>Total daily insulin dose (units/day) = 0.3 x weight (kg)</b></p> <p>All other patients <b>Total daily insulin dose (units/day) = 0.5 x weight (kg)</b></p> <p>Using insulin requirements during VRIL: assuming rate has been stable for last 6 hours <b>Total insulin over 6 hrs/ 6 x 20 = total daily dose</b></p>	<p>There is an adjustment for patients who may have impaired handling of insulin such as hepatic failure where the sensitivity is greater increasing the risk of hypoglycaemia</p> <p>The method calculated the average insulin requirement over 20 hours rather than 24 hours to prevent hypoglycaemia</p>
<p>When dividing the total daily dose</p> <ul style="list-style-type: none"> <li>- For basal bolus give 50% as the basal dose (evening) and 50% divided as short-acting insulins (breakfast, lunch and dinner)</li> <li>- For twice daily pre-mixed insulin regime give 60% with breakfast and 40% with evening meal</li> </ul>	<p>This is based on guidance for the Joint British Diabetes Society</p>





## APPENDIX A

### Types of Insulin

#### Long-acting insulins

- Insulin Degludec (Tresiba) ultra-long acting. Half-life 25 hours. Available in standard strength (100 units/ml) and concentrated (200 units/ml). Flexipens and standard cartridges.
- Insulin Detemir (Levemir).
- Insulin Glargine (Lantus).

#### Intermediate acting Insulins

- Isophane Insulin (Humulin I, Insulatard, Isophane)

#### Mixed Insulins

- Novomix 30 – 30% short acting, 70% intermediate acting
- Humalog mix 25 and Humalog 50 – number refers to % of short acting
- Humulin M – 30% short acting and 70% long acting

#### Short acting

- Soluble human insulin (Actrapid, Humulin S, Insuman rapid) natural human insulin. Acts within 30 minutes to an hour. When giving as part of basal bolus therapy it should be given 30 minutes before a meal.

#### Rapid acting

- Insulin Aspart (novorapid)
- Insulin Lispro (Humalog)
- Insulin glulisine (Apidra)

These insulins are rapid acting and work within minutes therefore should be given immediately before a meal



## APPENDIX B

# COncise adVice on Inpatient Diabetes (COVID:Diabetes): DEXAMETHASONE THERAPY IN COVID-19 PATIENTS: IMPLICATIONS AND GUIDANCE FOR THE MANAGEMENT OF BLOOD GLUCOSE IN PEOPLE WITH AND WITHOUT DIABETES

**DiABETES UK**  
KNOW DIABETES. FIGHT DIABETES.  
**JBDS** Joint British  
Diabetes Societies  
for inpatient care



## NATIONAL INPATIENT DIABETES COVID-19 RESPONSE GROUP\*

- i** This guidance is for use in ALL patients with COVID-19 who are treated with dexamethasone in a ward setting  
It is **NOT** intended for Critical Care Units but may be adapted for this use  
It differs from the previous COVID: Diabetes GUIDANCE FOR MANAGING INPATIENT HYPERGLYCAEMIA as it targets the greater insulin resistance in dexamethasone treated patients and should **ONLY** be used in this context

### ✓ Key Facts

- > Dexamethasone reduces mortality in people with COVID-19 who require ventilation or oxygen therapy
- > Corticosteroid therapy impairs glucose metabolism and is the commonest cause of life threatening inpatient Hyperglycaemic Hyperosmolar Syndrome (HHS)
- > COVID-19 increases insulin resistance and impairs insulin production from the pancreatic beta cells; this can precipitate hyperglycaemia and life threatening Diabetic Ketoacidosis (DKA) in people with diabetes and even in people not known to have diabetes
- > Glucose levels above 10.0 mmol/L have been linked to increased mortality in people with COVID-19
- > The recommended dexamethasone dose of 6mg/day (oral or IV) for 10 days, equivalent to 40mg of prednisolone/day, will undoubtedly affect glucose metabolism
- > Thus, the **triple whammy** of dexamethasone induced impaired glucose metabolism, COVID-19 induced insulin resistance and COVID-19 related impaired insulin production could result in significant hyperglycaemia, HHS and DKA in people with and without diabetes, increasing both morbidity and mortality
- > Sulphonylureas are NOT recommended in this context as beta cell function may be impaired and insulin resistance is likely to be severe. For this reason, these recommendations differ from those in the JBDS guideline on the Management of Hyperglycaemia and Steroid (Glucocorticoid) Therapy

### AIMS

- i** To ensure ALL patients on dexamethasone receive appropriate glucose surveillance and appropriate management of hyperglycaemia

### GLUCOSE MONITORING

Target glucose 6.0 -10.0 mmol/L (up to 12.0 mmol/L is acceptable)

#### Frequency of monitoring

##### > People not known to have diabetes

Check the glucose at least 6 hourly ideally at fasting periods (e.g. before meals and at bedtime). If after 48 hours all fasting glucose results are <10.0 mmol/L reduce frequency to once daily at 17.00-18.00 hrs. Continue until dexamethasone is stopped

If any fasting glucose is above 10.0 mmol/L continue 6 hourly monitoring and follow the guidance below to correct hyperglycaemia i.e. glucose above 12.0 mmol/L

##### > People with diabetes

Throughout the admission, check fasting glucose at least 6 hourly, or more frequently if the glucose is outside the 6.0 -10.0 mmol/L range







## MANAGING DEXAMETHASONE RELATED HYPERGLYCAEMIA

First, exclude Diabetic Ketoacidosis and Hyperglycaemia Hyperosmolar Syndrome by checking blood glucose, ketones, venous pH, bicarbonate and U&Es and if DKA/HHS diagnosed follow specific guidelines for their management

**▲ If DKA/HHS have been excluded, follow the guidance below but note, this advice is conservative. If after initial treatment hyperglycaemia persists, do not hesitate to escalate to the next treatment step and involve the diabetes team as early as possible**

### ADVICE FOR CORRECTING INITIAL HYPERGLYCAEMIA – GLUCOSE ABOVE 12.0 MMOL/L

Use **subcutaneous** rapid acting insulin analogue (Novorapid®/Humalog®/Apridra®) as described below. Note these are conservative doses and depending on response in individual patients, as previously stated, may need to be increased rapidly (or where more insulin sensitive, decreased)

Recheck glucose at 4 hrs to determine response and whether a further correction dose is needed

#### > Insulin naïve

Follow the weight-based tables below in those people:

- » not known to have diabetes
- » with type 2 diabetes treated with diet alone or with oral hypoglycaemic agents

#### > Insulin treated

Where the total daily dose (TDD) of insulin is known follow the guidance in the table based on TDD. If the TDD is unknown, follow guidance according to the person's weight

### CORRECTION DOSES OF RAPID ACTING INSULIN

GLUCOSE (MMOL/L)	TDD = <50 UNITS PER DAY • OR WEIGHT < 50 KG	TDD = 50 –100 UNITS PER DAY • OR WEIGHT 50 –100 KG	TDD = >100 UNITS PER DAY • OR WEIGHT >100 KG	
12.0-14.9	2 units	2 units	4 units	← • Please check <b>KETONES</b> if glucose >12.0mmol/L ▲ If <b>KETONE &gt;1.5mmol/L</b> , for doctor review ▲ If <b>KETONE &gt;3.0mmol/L</b> Exclude DKA-Venous pH, bicarbonate, lab glucose, U&E. Refer to diabetes team
15.0-16.9	2 units	3 units	5 units	
17.0-18.9	3 units	4 units	5 units	
19.0-20.9	3 units	5 units	6 units	
21.0-22.9	4 units	6 units	7 units	
23.0-24.9	4 units	7 units	8 units	
25.0-27.0	5 units	8 units	9 units	
Over 27	6 units	9 units	10 units	

### MAINTAINING GLYCAEMIC CONTROL

#### > People NOT on an intermediate acting (NPH) or long acting insulin:

Where glucose has risen above 12.0 mmol/L due to dexamethasone treatment, start NPH insulin which has an intermediate duration of action (e.g. Humulin I®, Insulatard®) - total dose 0.3 units/kg/day. Give 2/3 of the total daily dose in the morning (07.00 – 08.00) and the remaining 1/3 in the early evening (17.00-18.00). e.g. 0.3 x 80kg = 24 units/d i.e. 16 units a.m. and 8 units p.m.). NOTE- there should be a low threshold for dose escalation (see table below) and referral to the diabetes team

NPH insulin twice daily is recommended as this gives more flexibility with dose adjustment. However, the metabolic effects of dexamethasone can persist for up to 36 hours, thus a longer acting basal analogue insulin may also be considered. See tables below for dose adjustment of long acting insulin and twice daily intermediate and long acting insulins

#### ▲ ALERT NOTE - if:

- > Older (>70 yrs) or frail
- > Serum creatinine >175 umol/L (eGFR <30 ml/min)

Use a reduced NPH insulin dose of 0.15 units/kg (e.g. 0.15 x 80kg = 12 units i.e. 8 units a.m. and 4 units p.m.) NOTE- there should be a low threshold for dose escalation and referral to the diabetes team

#### > People already using once or twice daily long-acting insulin or twice daily NPH including those on basal-bolus regimens

Increase the long acting basal or NPH insulin by 20% but this may need rapid escalation by as much as 40% depending on response. Titrate the dose using the tables below. Patients on basal-bolus regimens may not require 'mealtime' insulin boluses if not eating, however, if hyperglycaemia persists during adjustment of basal insulin then use corrective rapid acting insulin doses according to total daily insulin dose (TDD) or weight given in the table for correction doses of rapid acting insulin





> **People on twice-daily pre-mix insulin**

e.g. NovoMix 30®/Humulin M3®/Humalog Mix 25®/Humalog Mix 50®

Continue mixed insulin and adjust dose (follow dose adjustment for long-acting insulin table below). Consider increasing the morning dose by 20% but this may need rapid escalation by as much as 40% each day depending on the response. There should be a low threshold for referral to the diabetes team

**DOSE ADJUSTMENT FOR LONG-ACTING INSULIN**

Doses can be titrated daily, although longer-acting insulins may take 48-72 hours to reach steady state. Dose adjustments will affect blood glucose throughout the day

**ONCE daily long-acting insulin**

GLUCOSE LEVEL JUST BEFORE INSULIN DOSE	
<4mmol/L	Reduce insulin by 20%
4.1-6mmol/L	Reduce insulin by 10%
6.1-12mmol/L	No change
12.1-18mmol/L	Increase insulin by 10%
>18mmol/L	Increase insulin by 20%

**TWICE daily NPH or long-acting insulin**

GLUCOSE LEVEL	JUST BEFORE MORNING INSULIN DOSE	JUST BEFORE EVENING INSULIN DOSE
<4mmol/L	Reduce <b>evening</b> insulin by 20%	Reduce <b>morning</b> insulin by 20%
4.1-6mmol/L	Reduce <b>evening</b> insulin by 10%	Reduce <b>morning</b> insulin by 10%
6.1-12mmol/L	No change	No change
12.1-18mmol/L	Increase <b>evening</b> insulin 10%	Increase <b>morning</b> insulin by 10%
>18mmol/L	Increase <b>evening</b> insulin by 20%	Increase <b>morning</b> insulin by 20%

> **People using a personal insulin infusion pump**

If the person is too unwell to manage their pump, transfer to a Variable Rate Intravenous Insulin Infusion (VRIII) with a basal insulin given alongside - seek the advice of the diabetes team. If the pump is removed, give the pump to a relative for safekeeping or label with the patients details and safely store

Those people well enough to manage their subcutaneous insulin infusion pump should be recommended to initially increase the basal rates by 20% and be made aware that this may need to be increased further on a daily basis. Refer all people using a personal insulin pump to the diabetes team

**END OF DEXAMETHASONE THERAPY- DAY 10**

Insulin resistance will begin to fall when the dexamethasone has been stopped but may take a number of days. Continue to monitor glucose 6 hourly and down titrate using the guidance table above

**DISCHARGE AND FOLLOW-UP**

> **Diabetes precipitated by COVID-19 infection and dexamethasone treatment**

Normoglycaemia may be established after stopping dexamethasone without the need for ongoing diabetes therapy. However, up to a third of people may later develop diabetes therefore alert the GP that the patient will need a yearly HbA1c measurement

> **People with known diabetes**

These patients will require close support following discharge. The discharge guidelines and patient information leaflet produced by this group are available to facilitate this. The leaflet can be accessed here: <https://www.diabetes.org.uk/professionals/resources/shared-practice/inpatient-and-hospital-care#patients>

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