NHS
Greater Glasgow and Clyde

CLINICAL GUIDELINE

Hyperglycaemia Hyperosmolar State (HHS)

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

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Lead Author	Steve Cleland
Approval Group	Area Drug and Therapeutics Committee

Important Note:

The Intranet version of this document is the only version that is maintained.
Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

MANAGEMENT OF HYPERGLYCAEMIC HYPEROSMOLAR STATE (HHS)

This NHSGGC Guideline and Care Pathway has been based on the Joint British Diabetes Societies (Inpatient Care Group) Guideline (2012), available to download at:
https://abcd.care/sites/abcd.care/files/resources/JBDS_IP_HHS_Adults.pdf

The complex pathophysiology and management of HHS means that **level 2 care** is usually most appropriate, with early input from specialist inpatient diabetes teams.

5 HEADLINE CONCEPTS:

(1) CORRECT DIAGNOSIS?

	HHS	Diabetic Ketoacidosis (DKA)
Age	Usually older	Usually younger
Volume depletion	10-20%	5-10%
Duration of onset	Days to weeks	Hours to days
Endogenous insulin	Usually present	Absent
Ketoacidosis	Absent / mild	Mild / moderate / severe

- HHS has slower onset than DKA, usually with no urgent need to clear ketoacidosis, and occurs in patients with brains at higher risk of injury by rapid shifts in sodium and glucose. Therefore, HHS requires less aggressive fluid resuscitation and glucose-lowering strategies than DKA

- Differentiating HHS from DKA is more problematic in context of severe intercurrent illness due to increased ketosis (eg SGLT2i, fasting ketosis) and non-ketotic metabolic acidosis (e.g. AKI*).* If predominant diagnosis unclear (HHS v DKA v both), then seek early specialist input to help tailor protocol to individual patient need.

(2) APPROPRIATE IV FLUIDS?

- Use intravenous (IV) **0.9%** sodium chloride to restore circulating volume and reverse dehydration (NB total body sodium is significantly deplete).
- Only switch to 0.45% sodium chloride solution if the osmolality is not declining (<3mOsm/kg/hour) despite adequate positive fluid balance.

- An initial rise in sodium is expected (reversal of relative pseudohyponatraemia in context of hyperglycaemia) and is not itself an indication for hypotonic fluids.
- The rate of fall of plasma sodium should not exceed 10 mmol/L in 24 hours.
- Aim for 2-3 litres positive balance by 6 hours and 3-6 litres positive balance by 12 hours.
- Consider less aggressive fluid resuscitation in context of low BMI (eg BMI<20), heart failure or oliguric renal failure.

(3) INSULIN – WHEN AND WHAT RATE?

- The fall in blood glucose should ideally be no more than 5 mmol/L/hour (so that serum osmolality doesn't fall too quickly). Low dose IV insulin should only be commenced
    - **EITHER** once the blood glucose level plateaus with IV fluids alone
    - **OR** immediately if there is significant ketosis (blood ketones > 1.5 or urine ketones greater than '+' (see Appendix A).

(4) TREATMENT TARGETS?

- If IV fluids and insulin are managed as above, serum osmolality should fall within the target range of 3-8mOsm/kg/hour.
- Ideally, laboratory-measured osmolality should be used, but calculated osmolality is adequate surrogate: **$2(Na^+ + K^+)$ + glucose + urea**.
- Failure to achieve this target increases risk of neurological complications such as cerebral oedema and pontine myelinolysis.

(5) OTHER ISSUES?

Remember also to:

(a) Correct other electrolyte deficiencies e.g. [Mg^{++}], [K^+], [Ca^{++}], [PO_4^{3-}]

(b) Prescribe prophylactic anticoagulation

(c) Investigate for and treat intercurrent illness e.g. sepsis

(d) Risk assess for pressure ulceration, especially in context of peripheral sensory neuropathy.

Name:

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Hyperglycaemic Hyperosmolar State (HHS): Care Pathway **1**

NHS Greater Glasgow and Clyde

Date: Time:

Weight (kg):

Default level of care = 2 (Medical High Dependency Unit), especially if any of these features:

Osmolality >350mosm/kg	Sodium >160mmol/L	H+ >80nmol/L
Hypo- or hyperkalaemia	Systolic BP <90mmHg	Heart rate >100 or <60bpm
Urine output <0.5ml/kg/hour	Creatinine >200µmol/L	Hypothermia
Acute Coronary Syndrome or stroke	Pregnancy	GCS <12
		Other serious co-morbidity

Step 1: Investigations

(initial when requested)	Initials
U&Es	
FBC	
Bicarbonate	
Venous blood gas	
Ketones: Capillary (CBK) or Urine (UK)	
Laboratory (not capillary) blood glucose	

Other interventions to consider

(initial if requested)	Initials
ECG or cardiac monitor	
Blood cultures	
CXR	
Record GCS	
MSSU	
Urinary catheter	

Step 2: Diagnosis for HHS

	Record result	Criteria	
Laboratory glucose		More than 30mmol/L	**Consider DKA if ALL criteria not met**
Calculate serum osmolality: **2 x (Na^++K^+) + glucose + urea**		More than 320mosm/kg	
Venous blood gas [H^+]		Less than 50nmol/L	
Venous bicarbonate		More than 15mmol/L	
Ketones: Capillary Blood (CBK) or Urine (UK)		Less than 3mmol/L (less than 3+)	

Step 3: Immediate Management: 0-60 minutes

(Initial when complete)	Initials
Commence 1L sodium chloride 0.9% over 1hour (caution if heart failure) or faster if systolic BP <90mmHg (see page 5)	
Only commence insulin if ketonaemia (>1.5mmol/L) or ketonuria (++ or more) (pg 6 and **APPENDIX A** for infusion rate details)	
Examine for source of sepsis or evidence of vascular event	
Mental state assessment (AMT 4 point)	
Ensure foot protection: 'Check / Protect / Refer' ('CPR') for feet	
Commence DVT prophylaxis (reduce enoxaparin dose to 20mg daily if <50kg or if eGFR<30ml/min)	
Continue long acting insulin and withhold oral diabetes medications	

Step 4: Ongoing Management: 60 minutes to 6 hours

(Initial when complete)	Initials
Commence insulin at 0.05 units/kg/hour ONLY IF blood glucose level plateaus on IV fluids (pg 6 and **APPENDIX A**)	
Ensure hourly CBG (capillary blood glucose). If CBG >28 or 'hi', use laboratory venous glucose. (record on page 11)	
Ensure U&Es, laboratory glucose and osmolality measured at 2hours then 4hourly thereafter (record on page 11)	
Continue sodium chloride 0.9% at a rate of 0.5-1 L/hour depending on clinical status and improvement of osmolality	
Ensure appropriate potassium replacement (see page 5)	
Once insulin commenced, commence IV Glucose 10% at a rate of 100mL/hour if glucose less than 14mmol/L (page 6)	

Step 5: Move to HHS Care Pathway 2 (page 7- STEP 6)

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Hyperglycaemic Hyperosmolar State (HHS) Care Pathway **1**: Prescribing

A. Fluid and Potassium Prescription

Fluid Replacement	Potassium Replacement

• Aim to achieve 2-3L positive fluid balance by 6hours and avoid a fall in sodium >10mmol/L in 24hours
• **Initial sodium rise expected**. If sodium increasing but osmolality declining (by more than 3mosm/kg/hour) – CONTINUE sodium chloride 0.9%
• If sodium increasing AND osmolality INCREASING (or less than 3mosm/kg/hour improvement), review fluid balance:
  ○ If inadequate fluid balance, CONSIDER increasing rate of infusion of sodium chloride 0.9%
  ○ If adequate fluid balance, CONSIDER switching to sodium chloride 0.45% at same rate
• If osmolality falling at more than 8mOsm/kg/hour CONSIDER reducing infusion rate of IV fluids and/or insulin if commenced.
	• Over 5.5mmol/L – no replacement
	• 3.5-5.5mmol/L – 40mmol replacement (max rate 10mmol/hour)
	• Below 3.5mmol/L – senior review as additional potassium required

PRESCRIPTION: INTRAVENOUS FLUIDS/POTASSIUM							ADMINISTRATION			
Date	Time	Name of fluid Name of additive	Vol (ml) Dose	Duration	Signature, PRINTED name and designation	Comment	Infusion started: Date	 Time	Given by	Check by
		Sodium chloride 0.9%	500ml	30mins						
		Sodium chloride 0.9%	500ml	30mins						
		Sodium chloride 0.9%	500ml							
		Sodium chloride 0.9%	500ml							
		Sodium chloride 0.9%	500ml							
		Sodium chloride 0.9%	500ml							
		Sodium chloride 0.9%	500ml							
		Sodium chloride 0.9%	500ml							
		Sodium chloride 0.9%	500ml							
STOPPED DATE:		**STOPPED BY (Prescriber's signature, PRINTED name and designation):**								

Fluid prescription chart continues on page 6

Name:

Date of birth: DD/MM/YYYY

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Hyperglycaemic Hyperosmolar State (HHS) Care Pathway **1**: Prescribing (cont'd)

PRESCRIPTION: INTRAVENOUS FLUIDS/POTASSIUM							ADMINISTRATION			
Date	Time	Name of fluid Name of additive	Vol (ml) Dose	Duration	Signature, PRINTED name and designation	Comment	Infusion started: Date	Infusion started: Time	Given by	Check by
STOPPED DATE:		STOPPED BY (Prescriber's signature, PRINTED name and designation):								

*****After 6 hours move to HHS Care Pathway 2: Prescribing (page 8)*****

B. Intravenous (IV) Insulin Prescription

- **Commence IV insulin ONLY IF blood glucose level plateaus on IV fluids or if significantly ketonaemic (see APPENDIX A for infusion rate details)**
- **Prescribe and administer insulin using the chart on pages 9 and 10. Prescribe 'As per chart' on Kardex.**

C. IV Glucose 10% Prescription

*****Only for patients on IV insulin with blood glucose < 14mmol/L, CONTINUE sodium chloride 0.9%*****

******If blood glucose rises to >15mmol/L: increase insulin rate by 1 unit per hour (with or without glucose 10%) to maintain a blood glucose target of 10-15mmol/L******

PRESCRIPTION: INTRAVENOUS GLUCOSE 10%							ADMINISTRATION			
Date	Time	Name of fluid	Vol (ml)	Duration	Signature, PRINTED name and designation	Comment	Infusion started: Date	Infusion started: Time	Given by	Check by
		Glucose 10%	**500ml**	**5 hours**						
		Glucose 10%	**500ml**	**5 hours**						
STOPPED DATE:		STOPPED BY (Prescriber's signature, PRINTED name and designation):								

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Hyperglycaemic Hyperosmolar State (HHS): Care Pathway **2**

STEP 6 Refer to inpatient diabetes team at the earliest opportunity

STEP 7 Read principles of treatment below

- HHS is associated with a significantly higher morbidity and mortality than DKA and must be managed intensively
- Fluid losses are estimated to be 10-22L in a person weighing 100kg
- Rate of fall of sodium should not exceed 10mmol/L in 24hours
- Complete normalisation of biochemistry, including other electrolyte deficiencies, may take 72hours
- Patients with HHS have a significantly higher risk of thromboembolism than in DKA and therefore all patients should receive prophylactic low molecular weight heparin (LMWH) for the duration of admission unless contra-indicated
- There is also a high risk of pressure ulceration

STEP 8 Ongoing Management: 6-12hours

(initial when complete)	Initials
Continue 4 hourly monitoring blood glucose, sodium, calculated osmolality and fluid balance (see table 1, record on p11)	
Assess for complications of treatment i.e. fluid overload, cerebral oedema, deteriorating conscious level	
Continue treatment of underlying cause, and replace other electrolyte deficiencies: [K^+], [Mg^{++}], [Ca^{++}], [PO_4^{3-}]	
Aim to keep blood glucose 10-15mmol/L	
Continue IV fluid replacement (see table 2 below and page 8 for prescribing chart)	

STEP 9 Ongoing Management: 12hours to resolution

(initial when complete)	Initials
Continue IV fluid replacement (see table 2) aiming to achieve replacement of estimated fluid losses within next 12 hours depending on initial degree of dehydration / body weight and MOST IMPORTANTLY response to treatment	
Continue keeping blood glucose 10-15mmol/L and adjust insulin infusion as appropriate (see table 1)	
Continue monitoring sodium (see table 1)	

Table 1: Reference Targets for HHS Management (6 hours to resolution)

Time	6hour	12hour	24hour	48hour	>48hour
Sodium	Improvement less than 5mmol/L	Not more than 5mmol/L improvement	Not more than 10mmol/L improvement	Not more than 20mmol/L improvement	Not more than 10mmol/L improvement/day
Osmolality	18-42mosm/kg improvement	36-96mosm/kg improvement	Continued improvement towards normal	Continued improvement towards normal	
Insulin	Commence if blood glucose level plateaus on IV fluids or significant ketonaemia (**APPENDIX A**) Reduce insulin rate if osmolality decreasing by more than 8mosm/kg/hour				
Fluid balance	2-3L positive balance	3-6L positive balance	Aim to replace remaining estimated losses		Neutral balance
Other	Ensure LMWH prescribed, pressure care, electrolyte correction, continuation of (appropriate) diabetes medications				

Table 2: IV Fluid and Potassium Replacement (prescribing chart on page 8)

Fluid Replacement	Potassium Replacement - first 24hours	Potassium Replacement > 24 hours
• Continue IV fluid replacement to achieve positive fluid balance of 3-6L by 12hours • Beyond 12hours, aim for IV fluid replacement aiming for replacement of estimated fluid losses over next 12 hours – dependent on initial degree of dehydration and response of treatment so far • Continue IV fluids thereafter until eating and drinking normally	• Over 5.5mmol/L – no replacement • 3.5-5.5mmol/L – 40mmol replacement (max rate 10mmol/hour) • Below 3.5mmol/L – senior review as additional potassium required	• Over 5.5mmol/L – no replacement • 3.5-5.5mmol/L – 10mmol replacement • Below 3.5mmol/L – 20mmol replacement

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Hyperglycaemic Hyperosmolar State (HHS) Care Pathway **2** : Prescribing

A. Fluid and Potassium Prescription (see table 2 on page 7)

PRESCRIPTION: INTRAVENOUS FLUIDS/POTASSIUM							ADMINISTRATION			
Date	Time	Name of fluid Name of additive	Vol (ml) Dose	Duration	Signature, PRINTED name and designation	Comment	Infusion started: Date	Infusion started: Time	Given by	Check by
STOPPED DATE:		STOPPED BY (Prescriber's signature, PRINTED name and designation):								

B. Intravenous Insulin Prescription (see table 1 on page 7 for guidance)

C. Glucose 10% Prescription

*****Only for patients on IV insulin with blood glucose < 14mmol/L, CONTINUE sodium chloride 0.9%*****

** If blood glucose rises to >15mmol/L: increase insulin rate by 1 unit per hour (with or without glucose 10%) to maintain a blood glucose target of 10-15mmol/L **

PRESCRIPTION: INTRAVENOUS GLUCOSE 10%							ADMINISTRATION			
Date	Time	Name of fluid	Vol (ml)	Duration	Signature, PRINTED name and designation	Comment	Infusion started: Date	Infusion started: Time	Given by	Check by
		Glucose 10%	500ml	5 hours						
		Glucose 10%	500ml	5 hours						
STOPPED DATE:		STOPPED BY (Prescriber's signature, PRINTED name and designation):								

Name:

Date of birth: DD/MM/YYYY

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Hyperglycaemic Hyperosmolar State: Intravenous insulin

Prescription, administration and monitoring chart

**** ONLY START IF BLOOD GLUCOSE LEVEL PLATEAUS OR IF KETONAEMIC – SEE APPENDIX A ****

1 Prescription details

Medicine	Total amount of insulin in syringe	Name of diluent	Total volume in syringe	Insulin concentration	Route	Prescriber's signature, PRINTED name and designation
SOLUBLE INSULIN (Actrapid® or Humulin S®)	50 units	Sodium Chloride 0.9%	50ml	1 unit/ml	IV	

2 Insulin flow rate details

	Date	Start time	Insulin dose (SEE APPENDIX A)	Required flow rate setting (ml/hour)	Additional instructions	Prescriber's signature, PRINTED name and designation
Commence if blood glucose level plateaus with IV fluids or significant ketonaemia – see APPENDIX A						
Initial rate						
Reduce rate if serum osmolality decreasing at more than 8mosm/kg/hour						
Change 1						
Change 2						
Change 3						
Change 4						

3 Preparation and pump set up details

	Date	Time	Preparation and pump set up by	Volume in syringe/bag (Post-priming)	Checked by
Initial prep					
Repeat 1					
Repeat 2					
Repeat 3					
Repeat 4					

4 Administration details (to be completed ONE hourly by nursing staff)

Date	Time	Volume remaining (ml)	Total volume infused (ml): cumulative	Volume infused since last check (ml)	Blood glucose reading (finger prick) mmol/L	Insulin flow rate prescribed (see section 2 above) ml/hour	Set by	Checked by	Site check (tick)	Comments

Name:

Date of birth: DD/MM/YYYY

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Hyperglycaemic Hyperosmolar State: Intravenous insulin

Prescription, administration and monitoring chart

****ONLY START IF BLOOD GLUCOSE LEVEL PLATEAUS OR IF KETONAEMIC – SEE APPENDIX A****

4 Administration details - continued (to be completed ONE hourly by nursing staff)

Date	Time	Volume remaining (ml)	Total volume infused (ml): cumulative	Volume infused since last check (ml)	Blood glucose reading (finger prick) mmol/L	Insulin flow rate prescribed (see section 2 above) ml/hour	Set by	Checked by	Site check (tick)	Comments

5. Discontinuation*

Prescriber's signature, PRINTED name and designation: **Date:** **Time:**

* Switch to appropriate s/c insulin when patient is eating, drinking and biochemical abnormalities have resolved. This should be done whenever practical following discussion with the diabetes team. Occasionally, if previously well controlled on oral agents or new presentation of diabetes, it may be appropriate to try oral agents.

Monitoring Record:

Name:

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Aim: to reduce osmolality by 3-8mosm/kg/hour

A: First 24 hours (See section C for ketones)

Time (hours)	0	2	6	10	14	18	22
Actual sample time							
Lab Glucose* **(mmol/L)**							
Sodium (mmol/L)							
Potassium (mmol/L)							
Urea (mmol/L)							
Creatinine (micromol/L)							
Osmolality (mosm/Kg)							
H^+ (nmol/L) **							

Record finger prick blood glucose in the table below** *[H^+] - frequency of monitoring may differ to table**

Capillary blood glucose in mmol/L : check hourly (lab venous glucose if CBG>28 or 'hi')

First 6 hours		7-12 hours		13-18 hours		19-24 hours	
Time	**Result**	**Time**	**Result**	**Time**	**Result**	**Time**	**Result**

B: After 24 hours

Date										
Actual sample time										
Lab Glucose (mmol/L)										
CBG (mmol/L)										
Sodium (mmol/L)										
Potassium (mmol/L)										
Urea (mmol/L)										
Creatinine (micromol/L)										
Osmolality (mosm/Kg)										
H^+ (nmol/L)										

C: Ketone monitoring

Capillary blood KETONES (CBK) in mmol/L														
Date	Time	Result	Date	Time	Result	Date	Time	Result	Date	Time	Result	Date	Time	Result

Appendix A:
When and how to start fixed-rate intravenous insulin infusions (FRIII) in HHS

Scenario 1 – HHS and CBK <1.5 (UK – or +)

- Do not start FRIII immediately
- Continue to monitor BG during IV fluid replacement (use laboratory venous BG if CBG '>28' or 'hi')
- If BG plateaus, commence FRIII at rate of 0.05 units/kg/hr (correct to nearest whole unit), aiming for target CBG 10-15

Scenario 2 – HHS and CBK ≥1.5 (UK >+) and [H^+] <50

- Start FRIII immediately at rate of 0.05 units/kg/hr (correct to nearest whole unit)
- Repeat BG (use laboratory venous BG if CBG '>28' or 'hi') and CBK at hourly intervals
- If BG decreasing too quickly (> 5mmol/l/hr), reduce FRIII rate by 50%
- Repeat BG and CBK regularly and, if necessary, adjust insulin rate to ensure both ketones are clearing and glucose is falling in a controlled manner, aiming for target CBG 10-15

Scenario 3 – HHS and CBK ≥1.5 (UK >+) and [H^+] ≥50

- Start FRIII immediately at rate of 6 units/hr (or 0.05 units/kg/hr, if weight >120kg - correct to nearest whole unit)
- Continue to monitor BG, CBK and [H^+] regularly and adjust insulin rate as required (be guided by insulin adjustment principles from the 'DKA protocol'), aiming for target CBG 10-15

IF IN DOUBT, SEEK URGENT INPUT FROM THE DIABETES TEAM

Abbreviations

HHS	Hyperglycaemic Hyperosmolar State
FRIII	Fixed-rate intravenous insulin infusion
BG	Blood Glucose
CBG	Capillary Blood Glucose level
CBK	Capillary Blood Ketone level
UK	Urinary Ketone level
[H+]	Hydrogen Ion level from venous or arterial blood gas analysis
DKA	Diabetic ketoacidosis