Guideline for the Management of Hyperosmolar Hyperglycaemic State (HHS) in Adults (previously known as Hyperosmolar Non-Ketotic Diabetic state (HONK))

University Hospitals of Leicester NHS
NHS Trust

Trust ref: B10/2018

1. Introduction

1.1. This document sets out the University Hospitals of Leicester (UHL) guidelines for the management of Hyperosmolar Hyperglycaemic State (HHS) in adults. It is based on the Joint British Societies (JBDS) guideline 'The Management of the hyperosmolar hyperglycaemic state (HHS) in adults with Diabetes' published in February 2022.

1.2. **Hyperosmolar hyperglycaemic state (HHS)** has no precise definition, but characteristic features that differentiate it from other hyperglycaemic states such as Diabetic ketoacidosis (DKA) are:

- marked hypovolaemia
- measured or calculated osmolality usually ≥ 320mosmol/kg
- marked hyperglycaemia (30mmol/L or more)
- without significant hyperketonaemia (blood ketones ≤ 3mmol/L)
- without significant acidosis (pH≥7.3, bicarbonate ≥ 15mmol/L)

N.B. A mixed picture of HHS and DKA may occur (see mixed DKA/HHS chart on page 4). Metabolic acidosis may be present in patients who are critically unwell.

1.3 The Goals of the treatment of HHS are to treat the underlying cause and to gradually and Safely:

- Normalise the osmolality
- Replace fluid and electrolyte losses
- Normalise blood glucose

Other goals include prevention of:

- Arterial or venous thrombosis
- Other potential complications e.g. cerebral oedema/central pontine myelinolysis /osmotic demyelination syndrome
- Foot ulceration

1.4. HHS can be a complex condition to manage and is associated with a significant mortality.

Diagnosis must be made promptly, treatment intensively monitored and the specialist diabetes team involved as soon as possible after admission.

1.5. Caution: in patients with Type 2 diabetes taking the class of oral hypoglycaemic agents

"SGLT-2 inhibitors". A risk of euglycaemic DKA has been identified with the use of 'SGLT-2 inhibitors'. If any patient is on an SGLT-2 inhibitor (eg, dapagliflozin, canagliflozin, empagliflozin or combination products, Xigduo, Vokanamet, Synjardy) and is unwell please consider DKA, rather than HHS even if blood glucose level is not significantly elevated. For criteria for diagnosis of DKA refer to UHL Guideline for the Management of Diabetic Ketoacidosis in Adults http://insitetogether.xuhl-tr.nhs.uk/pag/pagdocuments/Diabetic%20Ketoacidosis%20(DKA)%20in%20Adults%20UHL%20Guideline.pdf

2. Scope of the guideline

This guideline applies to all adult inpatients with Type 2 Diabetes and to all healthcare professionals who are responsible for the clinical management and/or care of these patients.

3. Recommendation,Standards and Procedural Statements

3.1 Definitions

3.1.1 **Hyperosmolar hyperglycaemic state (HHS)** The characteristic features of a person with HHS are marked hypovolaemia, measured or calculated osmolality usually ≥ 320mosmol/kg, marked hyperglycaemia (≥ 30mmol/L or more), without significant hyperketonaemia (ketones ≤ 3mmol/L), without significant acidosis (pH ≥7.3, bicarbonate ≥ 15mmol/L).

Treat as mixed DKA/HHS if the following is criteria are met. Start FRIII and IV fluids

Immediately and treat according to DKA pathway using 0.1 units/kg/hr

- marked hypovolaemia
- marked hyperosmolality
- pH <7.3 and
- blood ketones >3.0 mmol/L
- IV fluid replacement should aim to achieve a positive balance of 3-6 litres
- during the first 12 hours and the remaining replacement of estimated fluid
- loss during the following 12 hours, although complete normalisation of
- biochemistry may take up to 72 hours

Note: Usually HHS will be diagnosed and managed initially within the Emergency Department and LRI Acute Care Bay (ACB)/Acute Medical Unit. However, occasionally patients develop HHS whilst in hospital and this could occur in any ward area within UHL. Were this to occur please assess patient, initiate immediate treatment and discuss with medical SpR on-call regarding provision of care and on-going management.

3.1.2 **Definition of Resolution of HHS** It is difficult to give a precise definition of when HHS has resolved. It is important to remember that a normal glucose or sodium concentration in isolation is not sufficient to say that the episode has resolved. It can also be difficult to gauge the degree of dehydration at the bedside. However, we propose that a holistic approach be used, so resolution can be defined when -

- Measured or calculated serum osmolality falls to <300 mOsm/Kg,
- Hypovolaemia has been corrected (urine output ≥0.5 ml/kg/hr),
- Cognitive status is back to the pre-morbid state and
- Blood glucose <15 mmol/L

At that point we consider that HHS is no longer present.

3.2 Establishing the diagnosis of HHS

3.2.1 Suspect HHS in unwell patients with blood sugars ≥ 30mmol (for anyone with known Type 2 diabetes or previously unknown to have diabetes) and all 3 of the following are present:

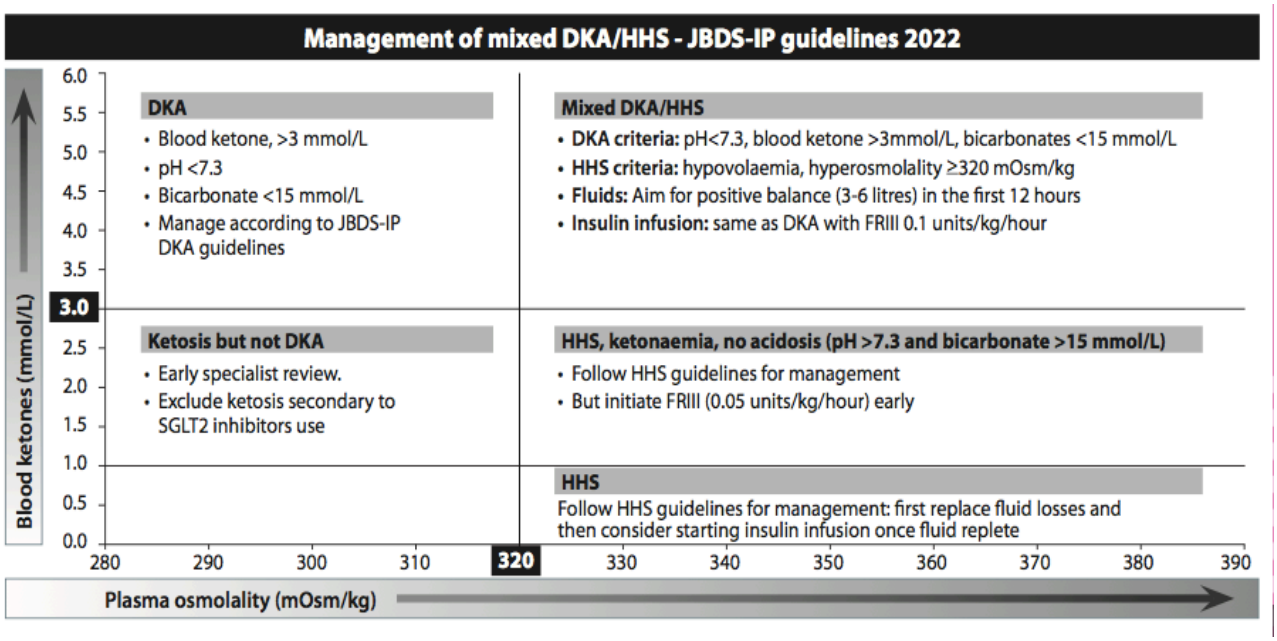
- High blood sugars without significant ketonaemia (blood ketones ≤3mmol/L or ketonuria < 2+) or acidosis (pH≥7.3, bicarbonate ≥ 15mmol/L)
- High Osmolality ≥ 320mosmol/kg*
- Hypovolaemia

***Calculated Serum osmolality = $2Na^+$ + glucose + urea: (NR 280-295mosmol/kg)**

If Type 1 diabetes or hyperglycaemia with acidosis (pH <7.3 or bicarbonate<15) AND ketones present (blood ketones>3mmol/L or ketonuria >2)

Or

Euglycaemic DKA, which has been identified with use of SGLT-2 inhibitors (see section 1.5) **THEN FOLLOW UHL DIABETIC KETOACIDOSIS (DKA) PROTOCOL**



3.2.2 The presence of one or more of the following may indicate severe HHS and need for admission to HDU/Level 2 environment.

IMMEDIATE senior review and consideration of admission to HDU/ITU should be considered if one or more of following present:

a) Measured or calculated Osmolality >350mosmol/kg

b) Pulse <60 OR >100 bpm

c) Serum sodium >160mmol/L

d) SaO2<92% on air (assuming normal baseline)

e) Venous or arterial pH<7.1

f) Serum creatinine > 200 µmol/L and/or acute kidney injury

g) Urine output < 0.5ml/kg/hr

h) Hypokalaemia (<3.5mmol/L) or hyperkalaemia (>6 mmol/l) on admission

i) Hypothermia

j) GCS< 12 (or abnormal AVPU score)

k) Macrovascular event such as acute MI or CVA

l) Systolic BP<90 mmHg

m) Other serious Co-morbidity

3.3 Special considerations

3.3.1 Serious complications may arise during the management of HHS as a result of treatment. These include:

a) Hypo or hyperkalaemia

b) Hypoglycaemia

c) Cerebral oedema

d) Pulmonary Oedema

e) Central pontine myelinolysis

3.3.2 It is critical that the patient and treatment are regularly monitored and reviewed as per Guidelines in order to minimise the risk of these complications

3.3.3 Groups of patients, in whom extra caution is required in their care and management particularly regarding fluid balance include:

a) Older people (>70yrs)

b) Cardiac or renal failure

c) Other serious co-morbidities

3.4 Provision of care for patients with HHS

3.4.1 Adult patients with suspected HHS admitted to the LRI Emergency Department (ED) should have the diagnosis confirmed and their treatment initiated in ED. Patients should then be transferred to the Acute Care Bay (ACB) LRI, or if clinically indicated, to ITU. If patients require stepdown from ACB to an appropriate medical ward this should be discussed and documented by either Diabetes SpR, Diabetes specialist in-reach team or medical SpR on-call.

3.4.2 If a patient with HHS is admitted to ED or ACB then the SpR or Consultant should be informed and the patient should be reviewed by a senior member of the team immediately if the NEWS indicates (see 3.2.2), or directly after clerking and initiation of treatment by a junior member of the team if NEWS does not indicate immediate senior review.

3.4.3 Patients who develop HHS in other LRI ward areas should have their treatment initiated according to this guideline by the ward team and should be reviewed by the Diabetes SpR or Medical SpR on-call as soon as possible and transfer to ACB should be arranged.

3.4.4 If HHS develops in a ward area at GGH or LGH then treatment should be initiated by the ward team and the patient should then be reviewed by the Diabetes SpR or Medical SpR on-call (depending on availability at each site) and a decision made regarding the appropriate area for the patient to be managed. In normal working hours (Mon-Fri, 9-5pm) there is a Diabetes SpR available to discuss cases (contact via switchboard).

3.4.5 If HHS develops outside of the ED or ACB then once immediate treatment has been initiated by the ward team referral for senior review (Diabetes SpR or Medical SpR on-call) should be made within the first hour of establishing diagnosis and initiating treatment.

3.5 **HHS care Pathway**

The following table details the HHS Care pathway divided into timed sections.

This pathway should be followed once a diagnosis of HHS has been established (see section 3.2)

Section A	Immediate management 0-60 minutes
Section B	60 minutes to 6 hours
Section C	6-12 hours
Section D	12-24 hours
Section E	24 hours to Day 3

HHS Care Pathway

Section A (0-60 mins)

Aims

Time = 0 mins at time intravenous (IV) fluids are commenced. If access problems, involve critical care support immediately

- Commence IV 0.9% sodium chloride – 1 litre over 1 hour
    - Consider more rapid replacement if SBP below 90 mmHg
    - Caution in the older people where too rapid rehydration may precipitate heart failure but insufficient may fail to reverse acute kidney injury
- Commence insulin infusion at presentation ONLY,

  If there is HHS and ketonaemia (blood ketone 3β-hydroxybutyrate level>1 mmol/ - ≤ 3mmol/L) and not acidotic (venous pH > 7.3 and bicarbonate > 15mmol/l), then use 0.05 units/kg/hr

  OR

  If there is significant ketonaemia (3β-hydroxybutyrate > 3mmol/l) or ketonuria (≥2+) with pH < 7.3 and bicarbonate <15mmol/L (i.e. mixed DKA and HHS) and use DKA guideline at 0.1 units/kg/hr

  Establish appropriate monitoring of patient (hourly capillary blood glucose, Na+, K+, urea and calculated osmolality)
- Perform clinical and biochemical assessment of patient

- Review IV fluid regimen based on patient's clinical and biochemical assessment, blood glucose levels and calculated osmolality

Action 1 – intravenous (IV) access and initial investigation and management

- Assess Airway, Breathing, Circulation and NEWS
- Site Large bore IV cannula
- Commence fluid replacement (for regimen see Action 2 below)
- Clinical assessment (RR,Temp,BP,Pulse, O2 SATS, NEWS score, GCS, full clinical examination including feet (assume high risk if patient obtunded or uncooperative) and mental state assessment
- Assess degree of dehydration, insert urinary catheter to monitor hourly urine output and calculate fluid balance
- Examine for source of sepsis or evidence of vascular event or recent medication changes?
- Initial investigations (capillary blood glucose (CBG), venous plasma BG, U&E, measured or calculated osmolality, venous blood gas, blood ketones, FBC, ECG, CXR, urine dip and if indicated MSU for culture) and CRP.
- Measured or calculated serum osmolality [(2xNa+) + glucose + urea]. Until the urea is available, calculate using (2xNa+ + glucose). Recalculate osmolality once urea is available, and then use (2xNa+ + glucose + urea).
- Blood cultures if clinically indicated
- Establish monitoring regime appropriate to patient, generally hourly for first 6 hours
  - Chart measured or calculated osmolality/glucose/sodium on HHS prescription chart
  - Continuous pulse oximetry
  - Consider continuous cardiac monitoring
- Commence prophylactic LMWH unless contra-indicated
- Consider IV antibiotics if sepsis identified or suspected
- Ensure heels are off-loaded
- Ensure daily foot checks
- Ensure early senior review and/or inform specialist diabetes team
- Confirm usual medication for diabetes and perform pregnancy test if appropriate

HHS Care pathway

Action 2 – restoration of circulating volume and potassium replacement

If Systolic BP < 90mmHG Consider more rapid replacement of 0.9% sodium chloride. A slower infusion rate should be considered in elderly patients (>70yrs) and those with renal/ cardiac failure (CVP may be considered in such groups).

When systolic BP > 90mmHg follow regimen in the table below if appropriate for patient.

Assessment of fluid balance, aiming to achieve positive fluid balance of 2-3L by 6 hours, should be part of the on-going management in all patients

Maintain potassium within normal range as follows:

POTASSIUM REPLACEMENT PRESCRIPTION ADVICE (use cardiac monitor)
Serum potassium concentration > 5.5mmol/L: no indication to replace

Serum potassium concentration < 5.5mmol/L: use 20mmol in 500mL 'premixed' bag

Note: fluid regime below is <u>a guide only</u> and should be amended according to patient's clinical status, osmolality and fluid balance. Review regularly and use clinical judgement.

	Fluid	**Volume over time**	**Rate (ml/hr)**
1st Litre	0.9% sodium chloride	1000ml over 1 hour	1000
2nd Litre	0.9% sodium chloride +/- potassium	1000ml over 2 hour	500
3rd Litre	0.9% sodium chloride +/- potassium	1000ml over 2 hour	500
4th Litre	0.9% sodium chloride +/- potassium	1000ml over 4 hour	250
5th Litre	0.9% sodium chloride or 0.45% sodium chloride +/- potassium	1000ml over 4 hour	250
Re-assessment of cardio-vascular status at 12 hours is mandatory, further fluid may be required			
6th Litre	0.9% sodium chloride or 0.45% sodium chloride +/- potassium	1000ml over 6 hour	166

Avoid hypoglycaemia

If capillary blood glucose falls to <14mmol/L then commence 10% glucose at 62.5ml/hr in addition to sodium chloride +/- potassium infusion. **Aim to keep capillary blood sugar between 10-15mmol/L in first 24hrs and avoid hypoglycaemia.**

Regular review of patient and clinical parameters is critical

HHS Care pathway

Action 3 Insulin therapy

- Commence at presentation ONLY if significant ketonaemia (blood ketone >1mmol/L or ketonuria >2+)
- Commence IV insulin **if** blood glucose level falling at rate < 5 mmol/L/hr despite adequate fluid replacement (see Action 2)
- Use IV human soluble insulin infusion (50 units in 50ml) at 0.05 units/kg/hr (e.g Actrapid or Humulin S)
- Modify IV insulin infusion rate as indicated (see Table below)
- If known to have diabetes and on treatment, review and <u>withhold whilst on IV insulin</u>
- Aim to keep blood glucose level 10-15mmol/L in first 24 hours

If CBG falls to < 14 mmol/L commence 10% glucose at 62.5ml/hr in addition to on-going fluid replacement

Weight (kg)	**IV insulin rate in unit/hour (based on 0.05unit/kg/hr)**
55	2.75 units/hr
60	3 units/hr
65	3.25 units/hr
70	3.5 units/hr
75	3.75 units/hr
80	4 units/hr
85	4.25 units/hr
90	4.5 units/hr

Action 4 – senior review

It is most important that patients with HHS are reviewed by medical a SpR/consultant immediately if NEWS indicates (see 3.2.2) or once immediate management has been initiated, if initially seen by a junior member of the team.

It is the role of the junior medical team and nursing staff to request a senior medical review in patients who develop HHS outside ED or ACB, the ward team should refer to the on-call SpR for Medicine or Diabetes SpR (depending on availability) within 1 hour of diagnosing HHS and initiating immediate treatment.

HHS Care Pathway

Section B (60mins- 6 hours)

Aims

- To achieve gradual decline in osmolality (3-8 mOsmol/kg/hr)
- To maintain potassium in normal range
- To avoid hypoglycaemia, aim to keep blood glucose 10-15 mmol/L in first 24 hrs
- Monitor vital signs and chart Medical Early Warning Score (NEWS)
- Maintain accurate fluid balance chart (minimum urine output 0.5ml/kg/hr)
- Ensure that senior review by SpR or Consultant has been undertaken

Action 1 – reassess the patient and monitor

- Review hourly initially, to ensure adequate progress in reducing osmolality and glucose levels is being made
- Ensure regular vital signs and NEWS charting and review
- Ensure accurate fluid balance charting (minimum urine output 0.5ml/kg/hr)

Action 2 – review metabolic parameters

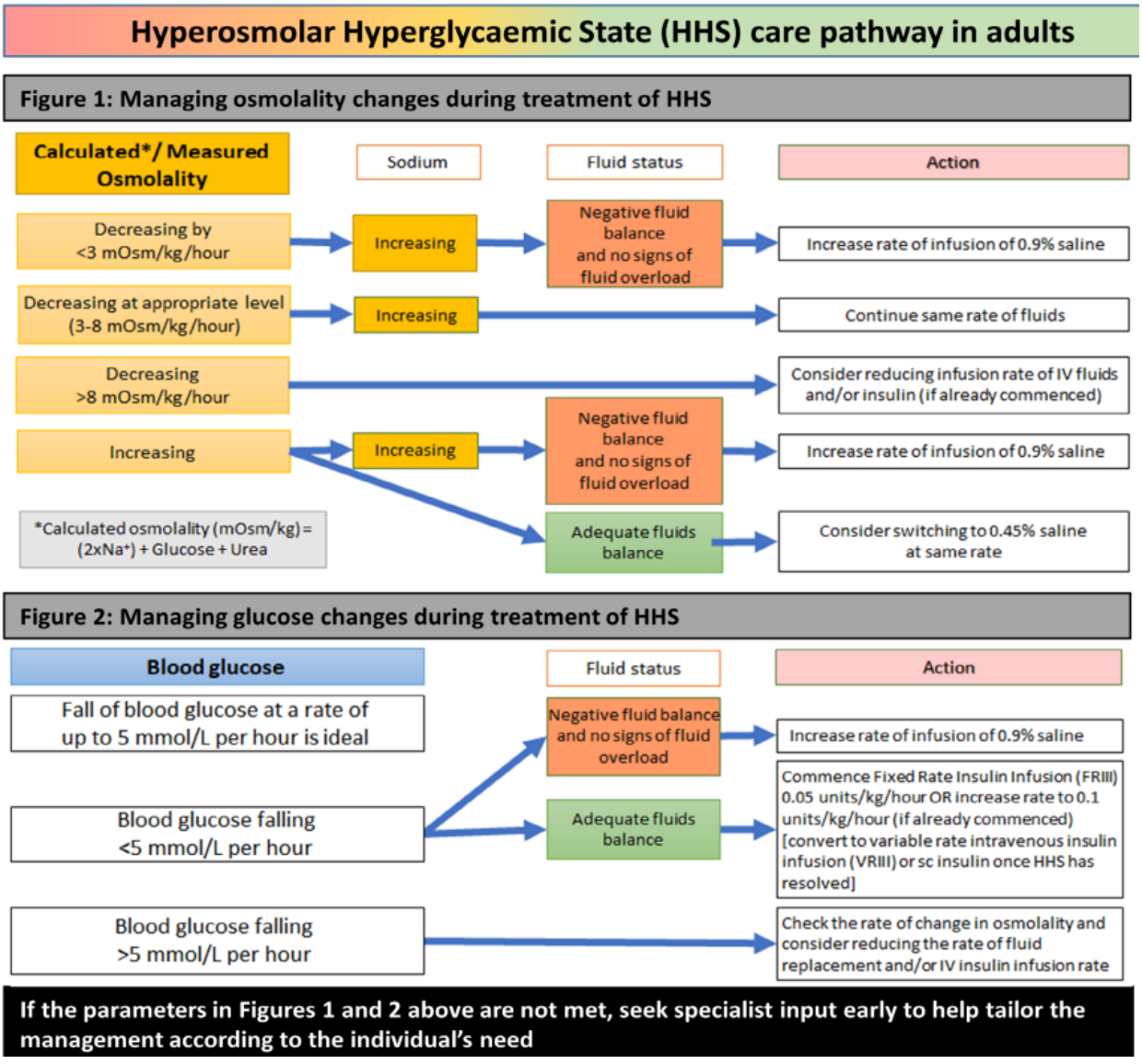
- Measure glucose, urea and electrolytes hourly and calculate osmolality ($2Na^+$ +glucose +urea) and record on HHS prescription chart.
    - If plasma Na^+ increasing but osmolality declining at appropriate rate, continue 0.9% sodium chloride
    - If plasma Na^+ increasing AND osmolality increasing (or declining at less than 3

mOsmol/kg/hr) check fluid balance. If positive balance is inadequate increase rate of infusion of 0.9% sodium chloride

- If osmolality increasing and fluid balance is adequate, consider switching to 0.45% sodium chloride at the same rate
- If osmolality falling at rate exceeding 8 mOsmol/kg/hr consider reducing infusion rate of IV fluids and/or insulin (if already commenced).

See flowchart on page 10.

- If blood glucose falling less than 5mmol/L check fluid balance
  - If positive balance is inadequate, increase rate of infusion of 0.9% sodium chloride
  - Fluid replacement should be adjusted for those who are <50 kg in body weight or with pre-existing heart and renal disease. More cautious fluid replacement is necessary e.g., 0.25 ml/kg/hr as recommended by NICE
  - Only start IV insulin once fluid balance is adequate and glucose concentrations have plateaued. Starting an IV insulin infusion too early could result in circulatory collapse. If fluid balance is adequate commence low dose IV insulin (0.05 units/kg/hr) or if already running, increase rate to 0.1units/kg/h



- Maintain potassium in normal range
- Hypokalaemia (less than 3.5 mmol/L) and hyperkalaemia (greater than 6 mmol/L) are life threatening conditions and warrant senior review. They are less common in HHS than DKA but

monitoring and replacement are essential

Potassium level in first 24 hr (mmol/L)	Potassium replacement in infusion solution
Over 5.5	Nil
3.5-5-5	40 mmol
Below 3.5	Senior review as additional potassium required

- Aim to keep blood glucose 10-15mmol/L in first 24 hours
    - If blood glucose falls below 14mmol/L commence 10% glucose at 62.5ml/hr AND CONTINUE 0.9% sodium chloride solution

HHS Care pathway

Section C (6-12 hours)

Aims

- Ensure that clinical and biochemical parameters are improving
- Continue IV fluid replacement to achieve positive balance of 3-6 litres by 12 hours
- Assess for and avoid complications of treatment (fluid overload, cerebral oedema, extra pontine myelinolysis e.g.,deteriorating consciousness level)
- Continue to treat precipitating causes
- Avoid hypoglycaemia

Action 1 – reassess the patient and monitor vital signs

- If not improving as desired (see section B), seek senior advice and contact on-call Diabetes SpR, if within working hours. If out of hours contact the on-call SpR for Medicine
- Ensure electronic referral (via ICE) is made to diabetes team – see Appendix B

Action 2 – review biochemical and metabolic parameters

- Continue charting blood glucose hourly; sodium and calculated osmolality 2 hourly
    - Take appropriate action (as outlined in Section B above)
- Maintain an accurate fluid balance chart
- Avoid hypoglycaemia
    - Aim to keep blood glucose 10-15mmol/L in first 24 hours
    - If blood glucose falls below 14 mmol/L commence10% glucose at 62.5ml/hr AND CONTINUE 0.9% sodium chloride solution

Section D (12-24 hours)

Aims

- Ensure continuing improvement of clinical and biochemical parameters
- Continue IV fluid replacement to achieve remaining replacement of estimated fluid losses within next 12 hours.
- Continue IV insulin with or without 10% glucose solution to maintain blood glucose 10-15mmol/L
- Assess for complications of treatment (fluid overload, cerebral oedema, extra pontine myelinolysis)
- Continue to treat precipitating causes

Action 1 – reassess the patient and monitor vital signs

- If not improving as desired (see section B), seek senior advice and contact on-call Diabetes SpR, if

within working hours. If out of hours contact the on-call SpR for Medicine

- Ensure electronic referral (via ICE) is made to diabetes team – see Appendix B

Action 2 – review biochemical and metabolic parameters

- Continue charting blood glucose hourly on prescription chart; sodium and calculated osmolality 4 hourly if improvement maintained (if not continue 2 hourly)
    - Take appropriate action (as outlined in Section B above) depending on results
    - Do not expect biochemistry to have normalised by 24 hrs (sodium and osmolality are likely to be raised)
    - Maintain an accurate fluid balance chart, plotting osmolality and make appropriate adjustments to fluid replacement rates
- Adjust insulin infusion rate hourly by 1 unit/hr increments or decrements to achieve desired CBG

HHS Care Pathway

Section E 24 hours to day 3

Expectation: patient should be steadily recovering, beginning to eat and drink, biochemistry returning to normal. See 3.1.2 for resolution criteria for HHS.

- Ensure that clinical and biochemical parameters are improving or have normalised
    - Continue IV fluids until eating and drinking normally
    - Switch to variable rate insulin if not eating and drinking when biochemically stable
    - Convert to appropriate subcutaneous insulin regime (Appendix A) if eating and drinking when biochemically stable
    - Encourage early mobilisation
    - Daily urea and electrolytes
    - Remove catheter when clinically appropriate
- Assess for signs of fluid overload or cerebral oedema
- Assess for evidence of continuing sepsis, review antibiotic prescription daily
- Daily foot checks
- Continue LMWH until day of discharge (consider extended treatment in very high risk patients)
- Ensure patient has been reviewed by a member of the diabetes team

Action 1 – conversion to subcutaneous insulin

- Convert to appropriate subcutaneous regime when biochemically stable
    - For those newly diagnosed with type 2 diabetes or new to insulin treatment, this should be managed by the diabetes team, but if not available (out of hours or at weekend) see Appendix A.
    - For patients who have previously been on s/c insulin see guidance in Appendix A

After care

- Most patients should go home on subcutaneous insulin
- For patients with previously undiagnosed diabetes or well controlled on oral agents, switching from insulin to the appropriate oral hypoglycaemic agent should be considered after a period of stability (weeks or months)
- Ensure patient has appropriate diabetes education prior to discharge and arrange follow-up by diabetes team

3.6. There are key recommendations/principles that are included in the JBDS Management of HHS Guidelines 2022 that differ from historic HONK guidance, these include:

a) Measuring or calculating osmolality ($2Na^+$ + glucose + urea) frequently to monitor the response to treatment.

b) Using (IV) 0.9% sodium chloride solution as the principal fluid to restore circulating volume and reverse dehydration. Only switching to 0.45% sodium chloride solution if the osmolality is not declining despite adequate positive fluid balance. An initial rise in sodium is expected and is not itself an indication for hypotonic fluids. Thereafter, rate of fall of plasma sodium should not exceed 10 mmol/L in 24 hours

c) The fall in blood glucose should be no more than 5 mmol/L/hr. Low dose IV insulin (0.05units/kg/hr) should be commenced once the blood glucose is no longer falling with IV fluids alone OR immediately if there is significant ketonaemia (3β-hydroxybutyrate (blood ketone level) greater than 1 mmol/L).

d) Assess foot risk on admission

Resolution criteria for HHS

4. Education and Training

4.1 It is expected that all registered staff working in the Emergency Department (ED), LRI admissions Acute Care Bay (ACB) and Diabetes Wards (LRI) have a responsibility to understand the management of HHS and up-date their knowledge. They will be supported by the Diabetes Team but staff would be expected to have undertaken Insulin Safety training (accessed via HELM) and familiarise themselves with this guidance.

4.2 All clinical staff working in any location within UHL would be expected to seek senior advice if they were presented with a patient with HHS and they did not feel adequately trained to manage the clinical case.

5. Monitoring and Audit Criteria

Outcome measures will be to benchmark the incidence of HHS against equivalent national and regional data for admissions. To assess adherence to the guidelines, outcome measures and effectiveness, audit will be performed periodically. The audit will be undertaken by the Diabetes Team.

Data relating to any incidents of inpatient HHS will be submitted to nationally data base NADIA Harms.

Monitoring and audit will be led by the Chair of the Diabetes Inpatient Safety Committee.

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
Audit of HHS admissions retrospectively to be undertaken one year after implementation	Against agreed standards taken from this guidance.		Initially after one year then 2 yearly thereafter	Diabetes inpatient safety committee

6. ***Supporting References***

1. Joint British Societies (JBDS) guideline 'The management of the hyperosmolar hyperglycaemic state (HHS) in adults with Diabetes' published in Feb 2022
2. *UHL guidelines for:*

- Prevention of Foot Complications and Management of Foot Ulcers in Patients with Diabetes – care plan(available on the UHL intranet as document 56006)
- Adult Anticoagulation, Thrombosis and Thromboprophylaxis Policy (available on the UHL intranet as document 25866)
- Guideline for the management of Diabetic ketoacidosis (DKA) in Adults**.** **http://insitetogether.xuhl-tr.nhs.uk/pag/pagdocuments/Diabetic%20Ketoacidosis%20(DKA)%20in%20Adults%20UHL%20Guideline.pdf**

Key Words

Hyperosmolar Hyperglycaemic State

HHS

Diabetes

Type 2

CONTACT AND REVIEW DETAILS	
Guideline Lead **Fiona Adlam, Advanced Specialist pharmacist Diabetes** **S Setty, Consultant Diabetologist**	**Executive Lead Andrew Furlong**

Details of Changes made during review:
Changes detailed in section 2

- **This document now emphasises that because more children and young people are being diagnosed with T2DM, and also presenting with HHS, there is a separate guideline for those under 18 years old, who are managed by paediatric teams. Please refer to UHL paediatric guidance on HHS.**
- **A new formal definition of resolution of HHS and audit standards has been included in this guidance.**
- **The core of the document – the 'How To' guide, remains essentially unchanged apart from minor changes to rate of fluids (Action 2, page 7)**
- **UHL HHS audit finding from 2020 highlighted certain areas of HHS care which needed additional support for the teams looking after patients with HHS. We have taken this opportunity to amend sections of the 'HHS prescription chart' to encourage better diagnosis, monitoring and management as shown below-**

Page1 –Establishing diagnosis of HHS (tick box section included)
Page 2- No changes
Page 3- has info on severity assessment and referral criteria for HDU/ITU. It also has additional HHS care pathway and a picture (mixed DKA/HHS) to complement abridges guidance on page 1 & 2
Page 4- has resolution criteria and revised monitoring chart.

Appendix A

Conversion to subcutaneous insulin

Where possible the conversion to subcutaneous insulin should be managed by the specialist diabetes team, especially for those with newly diagnosed type 2 diabetes (see point 4 below). Where this is not possible the following points give some guidance:

1. Restarting subcutaneous insulin for patients on an established insulin regimen

Previous regimen should be restarted

There should be a 30-60 min overlap between administration of the subcutaneous dose (of mixed insulin or mealtime 'bolus' insulin) and discontinuation of iv insulin infusion. This is because the half-life of iv insulin is only 3-4 mins and subcutaneous insulin may take considerably longer to be absorbed.
So the chain of events is:
 HHS resolved
 Patient starts eating and drinking
 Restart subcutaneous insulin (see below for timings)
 Stop IV insulin 30-60mins after s/c insulin

1.1 Patients on Basal Bolus regimen

Long acting or intermediate acting (aka NPH) insulin should have been stopped as per guideline recommendation
Do not stop IV insulin until some form of background/long acting insulin has been given.
For example if basal insulin is usually given at bed-time but you wish to restart subcutaneous insulin in morning, give ½ basal dose at breakfast with usual rapid acting insulin. Stop iv insulin infusion 30 mins later and continue with usual insulin regimen (e.g. normal meal time doses of rapid acting insulin plus the next full dose of long acting insulin may be given as usual).

1.2. Patients on twice daily mixed insulin

Re-introduce subcutaneous insulin before breakfast or evening meal and discontinue iv insulin infusion 30 mins after subcutaneous dose given.

2. Newly diagnosed type 2 diabetes

Do not stop IV insulin until some form of background insulin has been given.

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).
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.
Please ensure a referral to the Diabetes Nurse specialist/Diabetes Inreach is made, although this should not delay the commencement of s/c insulin. (Appendix B)

Appendix B

Referral guidelines for the Diabetes Specialist Team

 Electronic referrals to Diabetes Specialist Nurses are made via ICE (patient will be seen within one working day of receiving referral, as long as this falls within normal working hours)

 The Diabetes Specialist Nurses may also be contacted via the ‘Diabetes Nurse Helpline’ on x14919

 Referral to the on-call Diabetes SpR may be made via the LRI switchboard. Both available Mon-Fri (9am-5pm). **There is no out of hour’s diabetes on-call team.**

ADULT HYPEROSMOLAR HYPERGLYCAEMIC STATE (HHS) PRESCRIPTION CHART

NHS
University Hospitals of Leicester
NHS Trust

Patient's addressograph

For more information refer to UHL guidelines on HHS management. Abridged version available on page 2 of this chart. Monitoring chart on page 4.

ESTABLISH DIAGNOSIS OF HHS (All must be ticked to establish diagnosis)
***Assess severity (page 3) for ITU/level 2 care**

- ☐ Significant hypovolaemia
- ☐ Elevated osmolality ≥320 mOsm/kg - Calculate serum osmolality = (2Na+) + glucose + urea
- ☐ Marked hyperglycaemia (≥30 mmol/L without significant ketonaemia (blood ketones ≤3 mmol/L or ketonuria < 2+ or acidosis (pH ≥7.3) and HC03≥15)

Date ..... Ward ..... Patient's weight (kg) .....

1) INTRAVENOUS FLUIDS should be commenced via a large IV cannula (green or grey). If there is a problem with intravenous access critical care support should be requested immediately. Be aware of any fluids that may have already been given in the ambulance or ED.

Sodium chloride		Rate mL/hour (circle as appropriate)	Prescriber PRINT NAME	Administered by	2nd Nurse check	Time & date commenced
1st Litre over 1hr	Sodium chloride 0.9% 500ml/30mins	1000/other *.....				
	Sodium chloride 0.9% 500ml/30mins					

*** Rate depends on clinical assessment of dehydration/risk of precipitating heart failure and fluid balance (target is to achieve positive fluid balance of 2-3L by 6 hours). Review regularly and use clinical judgement, seek senior advice if unsure)**

	STANDARD INFUSION RATE; AMEND ACCORDING TO PATIENT FLUID STATUS	Rate mL/hour (circle as appropriate)	Potassium Check potassium & correct as appropriate (circle as appropriate)	Prescriber PRINT NAME	Administered by	2nd Nurse check	Time & date commenced
2nd Litre over 2hrs	Sodium chloride 0.9% 500ml/60mins	500/	Nil/20mmol in				
	Sodium chloride 0.9% 500ml/60mins	other.....	500ml other.....				
3rd Litre over 2hrs	Sodium chloride 0.9% 500ml/60mins	500/	Nil/20mmol in				
	Sodium chloride 0.9% 500ml/60mins	other.....	500ml other.....				
4th Litre over 4hrs	Sodium chloride 0.9% 500ml/2hrs	250/	Nil/20mmol in				
	Sodium chloride 0.9% 500ml/2hrs	other.....	500ml other.....				
5th Litre over 4hrs	Sodium chloride 0.9% or 0.45% 500ml/2hrs	250/	Nil/20mmol in				
	Sodium chloride 0.9% or 0.45% 500ml/2hrs	other.....	500ml other.....				
Re-assessment of cardio-vascular status at 12 hours is mandatory, further fluid may be required							
6th Litre over 4hrs	Sodium chloride 0.9% or 0.45% 500ml/2hrs	166/	Nil/20mmol in				
	Sodium chloride 0.9% or 0.45% 500ml/2hrs	other.....	500ml other.....				

**** Be aware of any fluids that may already have been given in the ambulance or ED. Use 1L sodium chloride 0.9% OR 1L 0.45%, depending on requirement. If using sodium chloride 0.45% and potassium replacement is required, then give potassium in pre-mixed bag with 5% or 10% glucose alongside.**

MONITOR PATIENT FOR FLUID OVERLOAD AND CEREBRAL OEDEMA
Any sudden deterioration in the patient's level of consciousness should be considered as likely cerebral oedema until definitively proven otherwise.

Risk of hypoglycaemia when blood sugar < 14 mmol/L prescribe 10% glucose 500ml at 125ml/hour to run alongside sodium chloride
Review rate of sodium chloride infusion to avoid fluid overload, e.g. likely to need to reduce rate of sodium chloride if 10% glucose running at 125ml/hr

	Rate mL/hour (circle as appropriate)	Prescriber PRINT NAME	Administered by	2nd Nurse check	Time & date commenced
10% glucose 500ml	125ml/other				
10% glucose 500ml	125ml/other				
10% glucose 500ml	125ml/other				
10% glucose 500ml	125ml/other				

2) POTASSIUM PRESCRIPTION ADVICE (use cardiac monitor)

Potassium level in first 24 hours	Potassium replacement in mmol / 500mL of infusion solution
Over 5.5mmol/L	Nil
3.5 to 5.5mmol/L	use 20mmol in 500mL 'premixed' bag
Less than 3.5mmol/L	Senior review

3) INSULIN THERAPY (Human soluble insulin e.g. Human Actrapid or Humulin S)
Commence at presentation ONLY if significant ketonaemia (blood ketone> 1mmol/L or ketonuria<2+). Commence IV insulin if capillary blood glucose (CBG) falling at rate < 5 mmol/L/hr despite adequate fluid replacement see below. Start IV soluble insulin infusion via a pump, containing 50 units soluble insulin in 50ml 0.9% sodium chloride at a continuous rate of 0.05 units/kg/hr. If known to have diabetes and is on anti-diabetic treatment (including insulin), withhold whilst on IV insulin. Monitor CBG, serum osmolality and serum sodium and adjust rate as per guidance overleaf. Aim to keep CBG 10-15mmol/L in first 24 hours. If CBG falls < 14 mmol/L commence 10% glucose at 125ml/hr.

INSULIN	Initial rate mL/hr 0.05 units/kg/hr	Prescriber PRINT NAME	Administered by	2nd Nurse check	Time & date commenced
Soluble Insulin 50 units in 50mL Sodium chloride 0.9%					
Soluble Insulin 50 units in 50mL Sodium chloride 0.9%					
Soluble Insulin 50 units in 50mL Sodium chloride 0.9%					

A mixed picture of HHS and DKA occurs frequently. Please see page 3 on how to manage.

Adapted from chart used at Countess of Chester Hospital NHS Foundation Trust

(Adlam)32314029SJ

Abridged ADULT HYPEROSMOLAR HYPERGLYCAEMIC STATE (HHS) MANAGEMENT GUIDELINES

Obtain IV access and commence fluid replacement immediately
If unable or poor IV access request critical care support immediately
Commence 0.9% sodium chloride – give 1 litre over 1 hour, consider more rapidly if systolic BP <90mm Hg (with caution in elderly)
Catheterise within first 60 mins to monitor fluid – aim minimum urine output 0.5ml/kg/hr

60 mins - 6 hours

Aim to achieve a gradual decline in osmolality of 3-8 mosmol/kg/hr. Use monitoring chart on Page 4.

- **Using 0.9% sodium chloride aim to give a further 0.5-1 L/hr depending on clinical assessment**

Targets:

- **A positive fluid balance of 2-3 litres by 6 hours**
- **A positive fluid balance of 3-6 litres by 12 hours**
- **Replacement of estimated fluid losses by 24 hour**

Provided osmolality declining appropriately, continue 0.9% sodium chloride (even if serum sodium increasing)

ADJUST RATES AS FOLLOWS: (Flow chart on page 3)
If osmolality increasing (or falling at rate <3mosmol/kg/hr) and serum sodium increasing, check fluid balance

- **If inadequate increase rate of 0.9% sodium chloride**
- **If adequate consider changing to 0.45% sodium chloride infused at same rate**

If osmolality falling at rate > 8mosmol/kg/hr (or > 3mosmol/kg/hr in those at risk of developing cerebral oedema), consider

- **Reducing rate of IV fluids**
- **Reducing rate of insulin infusion (if commenced)**

If Blood glucose falling by < 5 mmol/L/hr, check fluid balance

- **If inadequate increase rate of infusion of 0.9% sodium chloride**
- **If adequate commence low dose IV soluble insulin (0.05 units/kg/hr) or if already running, increase rate to 0.1 units/kg/hr**

Continue IV fluids until eating and drinking normally

Maintain potassium within normal range

Complete normalisation of electrolytes and osmolality may take up to 72 hours

Monitoring

- **Baseline investigations: capillary and venous CBG, capillary/urinary ketones, measured osmolality, venous blood gas, FBC, U+E, blood cultures, ECG, CXR, urinalysis and culture**
- **Establish a regime appropriate to patient**
- **Check Na^+, K^+, Urea, CBG and calculated osmolality every hour for first 6 hours then every 2 hours if response satisfactory**
- **Monitor vital signs and chart early Warning Score (EWS). Document accurate fluid balance chart**
- **The rate of fall of plasma Na^+ should not exceed 10mmol in 24 hours**
- **Use 24 hour HHS monitoring chart on page 3**
- **Assess for complications of treatment**

Other measures

- [ ] **Commence VTE prophylaxis (alternative if low eGFR) – follow trust protocol**
- [ ] **Consider IV antibiotics if sepsis identified or suspected – follow trust protocols**
- [ ] **Assess foot risk – assume high risk if uncooperative. Off load heels and ensure daily foot checks**
- [ ] **Assess mental state at baseline**

If known to have diabetes and is on anti-diabetic treatment (including insulin), withhold whilst on IV insulin

Assessment of severity

Care for people with HHS can be complex because they often have multiple co-morbidities and may require intensive monitoring.

The presence of one or more of the following should prompt discussion because they indicate they indicate the need for admission to a High-Dependency Unit / Level 2 environment:

- **Measured or calculated Osmolality >350 mOsm/kg**
- **Sodium >160 mmol/L**
- **Venous / arterial pH <7.1**
- **Hypokalaemia (<3.5 mmol/L) or Hyperkalaemia (>6mmol/L) on admission**
- **Glasgow Coma Scale (GCS) <12 or abnormal AVPU (Alert, Voice, Pain, Unresponsive) scale**
- **Oxygen saturation <92% on air (assuming normal baseline respiratory function)**
- **Systolic blood pressure <90 mmHg**
- **Pulse >100 or <60 bpm**
- **Urine output <0.5 ml/kg/hr**
- **Serum creatinine >200 umol/L and/or acute kidney injury**
- **Hypothermia**
- **Macrovascular event such as myocardial infarction or stroke**
- **Other serious co-morbidity**

HYPEROSMOLAR HYPERGLYCAEMIC STATE (HHS) CARE PATHWAY IN ADULTS

Figure 1: Managing osmolality changes during treatment of HHS

Calculated*/Measured Osmolality	Sodium	Fluid status	Action
Decreasing by <3 mOsm/kg/hour	Increasing	Negative fluid balance and no signs of fluid overload	Increase rate of infusion of 0.9% saline
Decreasing at appropriate level (3-8 mOsm/kg/hour)	Increasing		Continue same rate of fluids
Decreasing >8 mOsm/kg/hour			Consider reducing infusion rate of IV fluids and/or insulin (if already commenced)
Increasing	Increasing	Negative fluid balance and no signs of fluid overload	Increase rate of infusion of 0.9% saline
		Adequate fluids balance	Consider switching to 0.45% saline at same rate

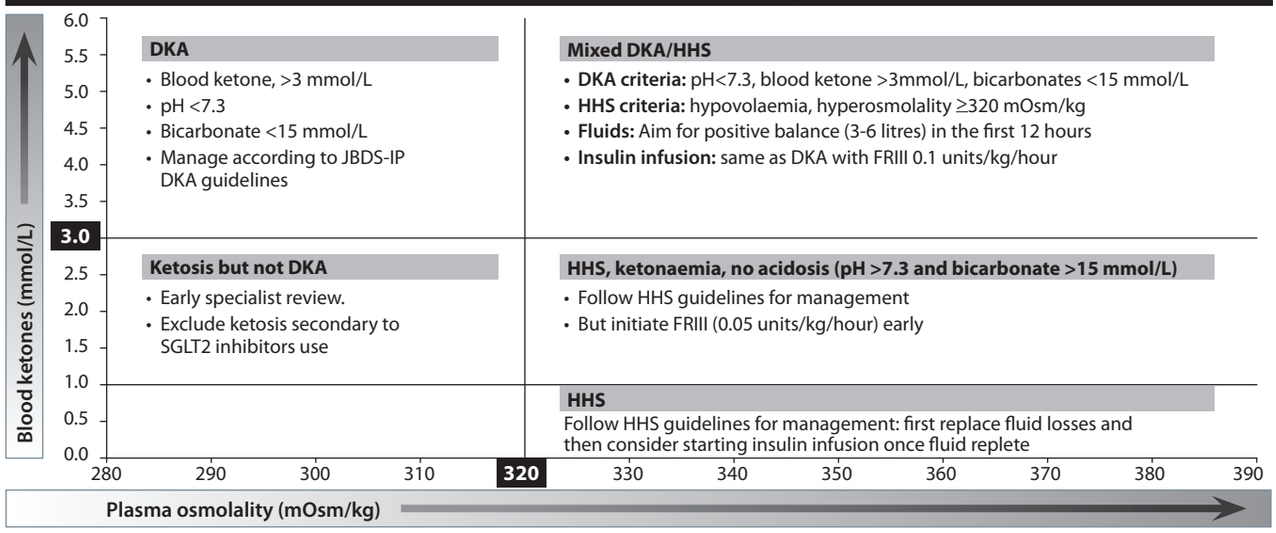
Calculated osmolality (mOsm/kg) = (2xNa) + Glucose + Urea

Figure 2: Managing glucose changes during treatment of HHS

Blood glucose	Fluid status	Action
Fall of blood glucose at a rate of up to 5 mmol/L per hour is ideal	Negative fluid balance and no signs of fluid overload	Increase rate of infusion of 0.9% saline
Blood glucose falling <5 mmol/L per hour	Adequate fluids balance	Commence fixed rate insulin infusion (FRIII) 0.05 units/kg/hour OR increase rate to 0.1 units/kg/hour (if already commenced) [convert to variable rate intravenous insulin infusion (VRIII) or sc insulin once HHS has resolved]
Blood glucose falling >5 mmol/L per hour		Check the rate of change in osmolality and consider reducing the rate of fluid replacement and/or IV insulin infusion rate

If the parameters in figures 1 and 2 above are not met, seek specialist input early to help tailor the management according to the individual's need

Management of mixed DKA/HHS - JBDS-IP guidelines 2022



ADULT HYPEROSMOLAR HYPERGLYCAEMIC STATE (HHS) PRESCRIPTION CHART

ADULT HYPEROSMOLAR HYPERGLYCAEMIC STATE (HHS) MONITORING CHART

Details:

Date .....

Ward .....

Treatment Aim:

- Improvement in clinical status and replacement of all estimated fluid losses by 24 hours
- Gradual decline in Osmolality: drop of 3-8 mOsm/kg/hr
- Blood glucose: aim to keep 10-15 mmol/L in the first 24 hrs
- Avoid hypoglycaemia and hypokalaemia
- Prevent harm

Resolution of HHS:

- ☐ Clinical/cognitive status back to pre-morbid state
- ☐ Osmolality normal (<300 mOsm/kg)
- ☐ Hypovolaemia corrected (UOP ≥0.5ml/kg/hr)
- ☐ Blood Glucose <15mmol/L
- ☐ Transfer to s/c insulin. See recovery phase

Monitor glucose. Sodium, potassium, urea and *calculated serum osmolality = 2 NA + glucose + urea (normal range 280-295 mOsm/kg) hourly for the first 6 hours. Then 2 hourly if response is satisfactory (i.e. a fall of 3.0-8.0 mOsm/kg/hr)

Date																							
Hours from start	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**
Sodium																								
Glucose																								
Urea																								
* Osmolality																								
Potassium																								
0.9% Sodium chloride ml/hr																								
0.45% Sodium chloride ml/hr																								
5% Glucose ml/hr																								
20% Glucose ml/hr																								
Urine output																								
Fluid balance																								
IV insulin rate (units/hr)																								

Recovery phase: IV insulin can usually be discontinued once patient is eating and drinking, but IV fluids may be required for longer if intake is inadequate. Complete correction of electrolytes and osmolality may take up to 72 hours. Ensure Specialist Diabetes Team review.