MANAGEMENT OF HYPONATRAEMIA IN ADULT INPATIENTS

This guidance does not override the individual responsibility of health professionals to make appropriate decisions according to the circumstances of the individual patient in consultation with the patient and / or carer. Health care professionals must be prepared to justify any deviation from this guidance.

INTRODUCTION

This guideline covers the investigations and treatment for hyponatraemia for adult inpatients.

THIS GUIDELINE IS FOR USE BY THE FOLLOWING STAFF GROUPS:

All qualified healthcare professionals who are involved in the investigation and treatment of adult inpatients with hyponatraemia.

Lead Clinician(s)

Dr R Bhaskar	Consultant Endocrinologist
Dr E Mitchell	Associate Divisional Director, SCSD
Hassan Yasin	Pharmacist ACP – Acute Medicine
Approved by Division of Medicine Clinical Governance Division of Surgery Clinical Governance	10th January 2025
Approved by Medicines Safety Committee	10th January 2025
Review Date:	10th January 2028
This is the most current document and should be used until a revised version is in place	

Key amendments to this guideline

Date	Amendment	Approved by:

INTRODUCTION

This guideline is to be used by qualified healthcare professionals to aid them in the investigation and treatment of hyponatraemia in adult patients. Hyponatraemia can potentially be a life-threatening biochemical abnormality and careful treatment is required to avoid the risk of further complications.

EPIDEMIOLOGY

Hyponatraemia is the most common electrolyte abnormality seen in clinical practice. It can result in a broad range of clinical symptoms, from mild to severe and potentially life-threatening. It is linked to higher mortality, increased morbidity, and longer hospital stays in patients presenting with various conditions. Hyponatraemia can be present in up to 15-20% of emergency admissions to hospital and occurs in up to 20% of critically ill patients.

CLASSIFICATION

This is based on the time of onset, the serum level and clinical signs/symptoms. The normal blood serum range for sodium is range is **133mmol/L– 146mmol/L.**

Onset	Duration
Acute	< 48 hours
Chronic	> 48 hours or unclear duration

Biochemical severity	Serum sodium (Na^+)
Mild hyponatraemia	130-135 mmol/L
Moderate hyponatraemia	125-129 mmol/L
Severe hyponatraemia	< 125 mmol/L.

CLINICAL FEATURES AND SEVERITY

Hyponatraemia is often asymptomatic**;** when symptoms are present, they are usually vague and non-specific. Symptoms/signs usually only occur when sodium levels are <125 mmol/L, with severe symptoms typically arising when levels drop below 120 mmol/L.

Severity	Signs/symptoms
Mild	asymptomatic or mild features of nausea, lethargy, irritability
Moderately severe	nausea, confusion, headache
Severe	vomiting, cardiorespiratory distress, abnormal and deep somnolence, focal neurological deficits, altered GCS, seizures, coma **Treat urgently (see page 9)**

AETIOLOGY

There are numerous causes of hyponatraemia and multiple mechanisms may contribute (e.g. medications, underlying heart failure, renal disease, SIADH). The assessment of fluid status is critical to determine the underlying cause of hyponatraemia.

Hypovolaemic hyponatraemia

- Gastrointestinal fluid loss
- Third spacing of fluids (bowel obstruction, sepsis, muscle trauma, pancreatitis)
- Diuretics
- Salt wasting nephropathies
- Cerebral salt wasting
- Mineralocorticoid deficiency
- Diabetes insipidus

Euvolaemic hyponatraemia

- Drugs
- SIADH
- Addisons disease
- Hypothyroidism
- High fluid intake

Hypervolaemic hyponatraemia

- Renal causes
- Heart failure
- Liver cirrhosis
- Iatrogenic

PSEUDO-HYPONATRAEMIA

False hyponatraemia can occur as an artefactual result due to a significant rise in serum proteins, serum lipids and/or glucose. This is termed pseudohyponatraemia.

POTENTIAL DRUG CAUSES

Stop any offending medications **depending on their clinical need** and/or consider alternative therapy. This is not an exhaustive list. Contact your ward pharmacist for more details.

Anticancer agents	Vinca alkaloids (e.g. Vincristine), platinum compounds (e.g. Cisplatin), Alkylating agents (e.g. Cyclophosphamide)
Anti-depressants	SSRIs (especially citalopram) Tricyclic antidepressants (e.g. amitriptyline), MAOI
Anti-epileptic medications	Carbamazepine, Sodium Valproate, Lamotrigine
Anti-hypertensives	ACEi, ARB
Anti-psychotic medications	Phenothiazines,
Diuretics	Thiazide diuretics (predominantly), Loop diuretics
Proton pump inhibitors	Omeprazole
Vasopressin analogues	Desmopressin, Oxytocin, Terlipressin
Others	Colonoscopy preparation (e.g. 'MOVIPREP'), 3,4-Methylenedioxymethamphetamine (MDMA)

DIAGNOSIS & INVESTIGATIONS

Urinary tests

- **Urinary osmolality**
- **Urinary sodium**
- **Urinary potassium**

Other (as indicated):

- **CT Head**
- **CXR**
- **Short synacthen test**

Blood tests

- **U&E**
- **Glucose**
- **Lipids**
- **Cortisol**
- **Thyroid function tests**
- **Liver function test**
- **Early morning cortisol**
- **Plasma/serum osmolality (gold topped tube)**

24-hour urine collection is not required as part of the initial management steps. Serum and urine osmolality are a common source of confusion – please see next page to aid with interpretation.

Serum and urine osmolality are important in determining the cause of euvolaemic hyponatraemia. In SIADH, the serum osmolality is typically low (i.e. < 275 mOsm/kg), urine osmolality is high due to an inability to dilute urine (i.e. > 100 mOsm/kg) and the urinary sodium is high (> 30 mmol/L). **However, it is important to remember that SIADH is diagnosis of exclusion.**

GENERAL MANAGEMENT OF HYPONATRAEMIA

MANAGEMENT IS DETERMINED BY

1. **Severity of symptoms.**
2. **Chronicity**: Acute (< 48 hours) or Chronic (> 48 hours). Treat as chronic if this is unclear and there are no severe symptoms.
3. **Volume status**.

IN ALL PATIENTS

1. Stop any **non-essential** offending medications (see page 3).
2. Assess fluid status
3. Review IV fluid chart
4. Treat the underlying cause
5. Ensure early involvement of ICU/hospital outreach team and involve senior medic if severe symptoms are present
6. Limit rise in sodium in first 24 hours to ≤ 10 mmol/L and ≤ 8 mmol/L in each following 24 hours.

INTERPRETING SERUM OSMOLALITY

High serum osmolality
Low serum sodium with serum osmolality > 295 mOsm/kg usually indicate relative dehydration, and/or may be due to marked hyperglycaemia.
High osmolarity may be due to administration of hypertonic, sodium poor fluids (mannitol)
Clinical signs of hypovolaemia may be present.

Normal osmolality
Low serum sodium with serum osmolality 275-295 indicates pseudo-hyponatraemia
This is often due to artifactually (falsely) low sodium concentration due to excessive protein (multiple myeloma) or lipid (hypertriglyceridaemia) interfering with the measurement of the sodium

Low osmolality
Low serum sodium with serum osmolality <275 mOsm/kg indicates hypotonic hyponatraemia. This is the most common form. Clinical signs of hypervolaemia are often present.

INTERPRETING URINE SODIUM CONCENTRATION AND URINE OSMOLALITY

This helps in understanding how much ADH (antidiuretic hormone) is being released. ADH causes the body to hold on to water, which makes the urine more concentrated, increasing its sodium levels and osmolality (a measure of how concentrated it is).

If Urine sodium is low (<30 mmol/l) AND Urine osmolality is high (> 100 mOsm/kg), this is the typical pattern for a body that can conserve sodium and water. This may be (patho) physiological.

- If the patient is HYPOvolaemic, consider: vomiting, burns, diarrhoea, sweating, or third space losses (e.g. pancreatitis, bowel obstruction, sepsis)
- If the patient is HYPERvolaemic, consider: heart failure, liver cirrhosis or nephrotic syndrome

If Urine Sodium is high (>30 mmol/l) and Urine Osmolality is high (>100 mmol/l) water is being conserved, but sodium is being wasted: Consider: SIADH, Diuretics (especially thiazides), hypothyroidism, Addisons disease.

Consider referral to endocrinology if:

- Suspected SIADH and for consideration of tolvaptan or demeclocycline
- Suspected adrenal insufficiency
- Patient is on desmopressin
- Deteriorating sodium levels or they remain static despite fluid restriction
- Patient unable to comply to fluid restriction
- Diagnosis is uncertain despite investigations

Email: wah-tr.diabetesandendocrinereferrals@nhs.net
or for more urgent advice, contact Endocrine registrar via switchboard.

MANAGEMENT OF ACUTE HYPONATRAEMIA (<48 hours) WITHOUT SEVERE SIGNS/SYMPTOMS

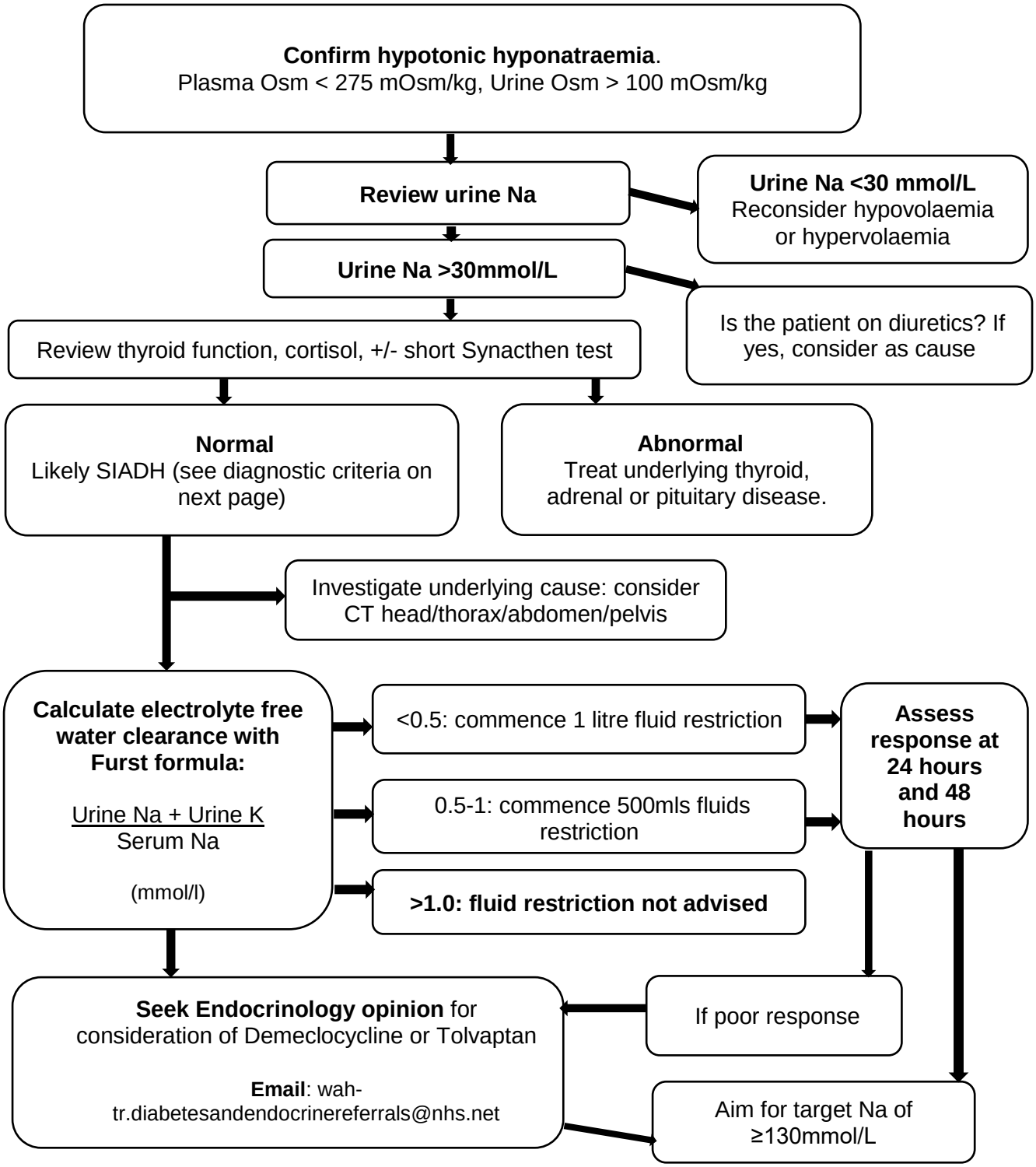
- Ensure there are no sampling or sample handling errors e.g. drip arm venepuncture. Recheck sodium.
- Stop any non-essential fluids or medication that could be contributing/provoking (see page 3).
- Make diagnostic assessment and treat underlying cause.
- If hypovolaemic start IV 0.9% sodium chloride.
- Recheck sodium after 4 hours to determine trend.
- Limit rise in sodium in first 24 hours to ≤ 10 mmol/L and ≤ 8 mmol/L in each following 24 hours.

MANAGEMENT OF CHRONIC HYPONATRAEMIA (> 48 HOURS OR UNCLEAR DURATION) WITHOUT SEVERE FEATURES

ASSESS VOLUME STATUS

Hypovolaemia Reduced skin turgor, low BP or postural hypotension.	**Restore volume with IV 0.9% sodium chloride.** In haemodynamic compromise the need for rapid fluid resuscitation overrides the risk of an overly rapid increase in sodium
Euvolaemia	**See page 7**
Hypervolaemia Oedema, raised JVP, ascites.	**Treat the underlying cause.** Consider fluid restriction to prevent further fluid overload.

ALGORITHM FOR THE MANAGEMENT OF CHRONIC EUVOLAEMIC HYPONATRAEMIA WITHOUT SEVERE FEATURES



Adapted, with permission from *Guidelines for the Initial Assessment and Management of Hyponatraemia in Adults - Nottingham University Hospitals NHS Trust, October 2022.*

Diagnostic Criteria for SIADH

- Clinically euvolaemic

- Serum osmolality < 275 mOsm/Kg
- Inappropriately concentrated urine > 100 mOsm/Kg, usually > 300 mOsm/Kg
- Increased urine Na+ (> 30 mmol/L)
- Absence of adrenal, thyroid, pituitary, or renal insufficiency
- INTERPRET BIOCHEMISTRY WITH CAUTION IF PATIENT IS ON DIURETIC THERAPY

Demeclocycline (Must be authorised by Endocrine consultant or registrar).
Initial dose: 900-1200mg daily in divided doses (e.g. 300mg - 400mg TDS)
Maintenance dose: 600-900mg daily in divided doses
Should be swallowed whole with plenty of fluid while sitting or standing. Doses should be taken an hour before or 2 hours after meals. Absorption is impaired by milk and food. Inform ward Pharmacist so supply can be obtained.

Contraindications: acute porphyria, pregnancy or breastfeeding, children under 12 years of age, patients with a history of hypersensitivity to tetracycline.

Warnings: May increase muscle weakness in patients with myasthenia gravis. Exacerbation of pre-existing SLE has been reported with tetracyclines. Patients who have known liver disease should not receive more than 1g daily. Lower doses are indicated in cases of renal impairment (seek advice from ward Pharmacist and see below).

GFR (ml/min) 20-50: dose as in normal renal function
GFR (ml/min) <20: maximum 600mg every 24-48 hours

Demeclocycline has the greatest potential of the tetracycline class for causing photo-allergic reactions in hypersensitive persons. Such patients should be warned to avoid direct exposure to natural or artificial sunlight and to discontinue therapy at the first sign of skin discomfort.

Tolvaptan (Must be authorised by Endocrine consultant or registrar).

- Remove any fluid restriction and allow patient to drink to thirst response
- 'Samsca ®' oral tablets are the only licensed brand of tolvaptan for the treatment of SIADH.
- Initiate at a dose of 7.5mg. Repeat Na+ 6 hours later
- Repeat dose if no improvement after 24 hours. If there is no improvement after the second dose, then reconsider diagnosis.
- Prescribe on the STAT section of the drug chart as only one or two doses may be required to correct sodium levels back to normal. Do not prescribe on the regular side of the chart. Inform ward Pharmacist so supply can be obtained.
- Tolvaptan dosing is once daily, compared to multiple daily dosing for demeclocycline
- Caution should be exercised in co-administering CYP3A4 inhibitors (e.g., ketoconazole, macrolide antibiotics, diltiazem). Avoid grapefruit juice.
- Exercise caution in co-administration of CYP3A4 inducers (e.g., rifampicin, barbiturates). Discuss drug interactions with pharmacist.

MANAGEMENT OF SEVERE HYPONATRAEMIA

IF SEIZURES, COMA, ALTERED GCS OR ENCEPHALOPATHY START URGENT TREATMENT AS BELOW (REGARDLESS OF CHRONICITY AND CAUSE).
This is a medical emergency.

Severe features of hyponatraemia usually only occur when serum sodium levels are <120mmol/L. If serum levels are above 120mmol/L, please also consider other causes for the symptoms.

The primary treatment aim is to **improve symptoms rather than to restore sodium levels to normal.**

FIRST HOUR MANAGEMENT:
1. *Give 150 mls IV 2.7% sodium chloride (hypertonic saline) over 20 minutes. It can be given through a peripheral cannula, although central access is preferable.
2. *Ensure early involvement of ICU/hospital outreach team and involve senior medic.
3. Check sodium concentration; continue treatment below while awaiting result.
4. Give 150 mls IV 2.7 % sodium chloride over 20 minutes until sodium risen by 5 mmol/L or repeated twice.
5. Serum sodium should be monitored hourly over the first 24 hours if patients require more than two boluses of 2.7% saline without improvement in symptoms, otherwise 6 hourly for the first 24 hours.

Seek expert advice if patient fluid overloaded with pulmonary oedema.

SUBSEQUENT MANAGEMENT:
1. Stop 2.7% sodium chloride.
2. Slow IV infusion 0.9% sodium chloride.
3. Start diagnosis specific treatment.
4. Limit rise in sodium in first 24 hours to ≤ 10 mmol/L and ≤ 8 mmol/L in each following 24 hours.
5. Recheck sodium at 6, 12, 24 and 48 hours.

*Discuss all patients who require hypertonic saline with critical care. It is recommended that this is given via a central line due to the risk of extravasation injury. However, do not defer the administration of hypertonic saline if a peripheral cannula is available and timely administration is necessary, or central access is not clinically appropriate. Ideally use a wide bore, free flowing cannula for peripheral administration. Observe carefully for signs of extravasation. Do not defer treatment of symptomatic severe hyponatraemia until critical care arrive.

If 2.7% strength is unavailable or there are concerns regarding vein patency, then 1.8% sodium chloride can be considered.

COMPLICATIONS

Cerebral Oedema (usually a complication of correcting HYPERnatraemia, or resulting from acute water overload causing HYPOnatraemia)
This occurs to water moving into brain cells in acute hyponatraemia, leading to increased intracranial pressure. Symptoms can include headache, nausea, vomiting, confusion, seizures, and even coma. Usually requires rapid correction.

Osmotic Demyelination Syndrome (ODS)
Also known as central pontine myelinolysis, this rare complication occurs when sodium levels are corrected too quickly. It causes damage to nerve cells, leading to weakness, difficulty speaking and swallowing, and potentially permanent neurological deficits.

Patient groups at higher risk of ODS: elderly, children <16, malnourished, alcoholics, CNS disease and post-operative patients. May need to consider correcting sodium levels more slowly in these groups. Cautious management (as outlined in this guideline) is crucial in correcting sodium levels slowly and steadily, to avoid complications like ODS. Regular monitoring of sodium levels, fluid balance, and clinical status are essential in high-risk patients.

References

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Clayton, J., 2023. *Guidelines for the initial assessment and management of hyponatraemia in adults*. Nottingham University Hospitals NHS Trust. Available at: https://nuhp.koha-ptfs.co.uk/cgi-bin/koha/opac-retrieve-file.pl?id=786cc3d7d2e296257072bbf1dcdc2ef7 [Accessed 18 December 2024]

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Spasovski, G. et al., 2014. Clinical practice guideline on diagnosis and treatment of hyponatraemia. *European Journal of Endocrinology*, 170(3), pp.G1–G47. Available at: https://academic.oup.com/ejendo/article/170/3/G1/6668028 [Accessed 18 December 2024].

Contribution List

This key document has been circulated to the following individuals for consultation;

Designation
Mr. N Purser, Clinical Governance Lead for Surgery
Dr W Foster, Associate Divisional Director for Medicine
Kavitha Ganapathy, Endocrine Registrar

This key document has been circulated to the chair(s) of the following committee's / groups for comments;

Committee
Medicines Safety Committee.

Supporting Document 1 - Equality Impact Assessment Tool

To be completed by the key document author and included as an appendix to key document when submitted to the appropriate committee for consideration and approval.

Please complete assessment form on next page;

NHS Worcestershire Acute Hospitals NHS Trust

Herefordshire & Worcestershire STP - Equality Impact Assessment (EIA) Form
Please read EIA guidelines when completing this form

Section 1 - Name of Organisation (please tick)

Herefordshire & Worcestershire STP		Herefordshire Council		Herefordshire CCG	
Worcestershire Acute Hospitals NHS Trust	X	Worcestershire County Council		Worcestershire CCGs	
Worcestershire Health and Care NHS Trust		Wye Valley NHS Trust		Other (please state)	

Name of Lead for Activity	**Dr E Mitchell**

Details of individuals completing this assessment	**Name**	**Job title**	**e-mail contact**
	Dr E Mitchell	**Consultant in Intensive Care**	**Ed.mitchell@nhs.net**
Date assessment completed	**17.10.24**		

Section 2

Activity being assessed (e.g. policy/procedure, document, service redesign, policy, strategy etc.)	**Clinical Guideline for the investigation and management of hyponatraemia**

What is the aim, purpose and/or intended outcomes of this Activity?	Emergency treatment of hyponatraemia			
Who will be affected by the development & implementation of this activity?	X❑ X❑ ❑ ❑	Service User Patient Carers Visitors	X❑ ❑ ❑ ❑	Staff Communities Other _____
Is this:	X❑ Review of an existing activity ❑ New activity ❑ Planning to withdraw or reduce a service, activity or presence?			
What information and evidence have you reviewed to help inform this assessment? (Please name sources, e.g. demographic information for patients / services / staff groups affected, complaints etc.	Document content sourced from NICE			
Summary of engagement or consultation undertaken (e.g. who and how have you engaged with, or why do you believe this is not required)	Not required as this is implementation of national level advice.			
Summary of relevant findings	No negative consequences identified			

Section 3

Please consider the potential impact of this activity (during development & implementation) on each of the equality groups outlined below. **Please tick one or more impact box below for each Equality Group and explain your rationale**. Please note it is possible for the potential impact to be both positive and negative within the same equality group and this should be recorded. Remember to consider the impact on e.g. staff, public, patients, carers etc. in these equality groups.

Equality Group	Potential positive impact	Potential neutral impact	Potential negative impact	Please explain your reasons for any potential positive, neutral or negative impact identified
Age	X			Hyponatraemia more common in elderly patients who experience more symptoms and morbidity from the condition. This guideline will improve health outcomes for this group.
Disability		X		

Equality Group	Potential positive impact	Potential neutral impact	Potential negative impact	Please explain your reasons for any potential positive, neutral or negative impact identified
Gender Reassignment		X		
Marriage & Civil Partnerships		X		
Pregnancy & Maternity		X		
Race including Traveling Communities		X		
Religion & Belief		X		
Sex		X		
Sexual Orientation		X		
Other Vulnerable and Disadvantaged Groups (e.g. carers; care leavers; homeless; Social/Economic deprivation, travelling communities etc.)	X			Hyponatraemia more common in disabled and chronically unwell groups of patients. This guidance will preferentially be applicable to this group of patients.
Health Inequalities (any preventable, unfair & unjust differences in health status between groups, populations or individuals that arise from the unequal distribution of social, environmental &	X			Hyponatraemia more common in patients with higher rates of social deprivation and the diseases this brings e.g. cirrhosis, heart failure, acute alcohol abuse, cancer. This guideline will improve access to treatment for this group.

Equality Group	Potential positive impact	Potential neutral impact	Potential negative impact	Please explain your reasons for any potential positive, neutral or negative impact identified
economic conditions within societies)				

Section 4

What actions will you take to mitigate any potential negative impacts?	Risk identified	Actions required to reduce / eliminate negative impact	Who will lead on the action?	Timeframe
		.		
How will you monitor these actions?	**Monitoring of severe incidents through incident reporting Monitoring of deaths from electrolyte disurbance**			
When will you review this EIA? (e.g. in a service redesign, this EIA should be revisited regularly throughout the design & implementation)	**January 2028**			

Section 5 - Please read and agree to the following Equality Statement

1. Equality Statement

1.1. All public bodies have a statutory duty under the Equality Act 2010 to set out arrangements to assess and consult on how their policies and functions impact on the 9 protected characteristics: Age; Disability; Gender Reassignment; Marriage & Civil Partnership; Pregnancy & Maternity; Race; Religion & Belief; Sex; Sexual Orientation

1.2. Our Organisations will challenge discrimination, promote equality, respect human rights, and aims to design and implement services, policies and measures that meet the diverse needs of our service, and population, ensuring that none are placed at a disadvantage over others.

1.3. All staff are expected to deliver services and provide services and care in a manner which respects the individuality of service users, patients, carer's etc, and as such treat them and members of the workforce respectfully, paying due regard to the 9 protected characteristics.

Signature of person completing EIA	E M Mitchell
Date signed	10.03.2025
Comments:	

Signature of person the Leader Person for this activity	
Date signed	
Comments:	

Supporting Document 2 – Financial Impact Assessment

To be completed by the key document author and attached to key document when submitted to the appropriate committee for consideration and approval.

	Title of document:	Yes/No
1.	Does the implementation of this document require any additional Capital resources	No
2.	Does the implementation of this document require additional revenue	No
3.	Does the implementation of this document require additional manpower	No
4.	Does the implementation of this document release any manpower costs through a change in practice	No
5.	Are there additional staff training costs associated with implementing this document which cannot be delivered through current training programmes or allocated training times for staff	No
	Other comments:	

If the response to any of the above is yes, please complete a business case and which is signed by your Finance Manager and Directorate Manager for consideration by the Accountable Director before progressing to the relevant committee for approval.