GDL13
The use of potassium binders in the management of persistent hyperkalaemia in patients with cardiorenal syndrome

1.0 Procedure Statement

To advise members of the cardiorenal MDT (cardiologists, nephrologists, heart failure nurses, acute kidney injury nurses, cardiology pharmacists, renal pharmacists) on the management of hyperkalemia in patients with cardiorenal syndrome. These guidelines DO NOT replace the Trust Hyperkalaemia guidelines.

2.0 Accountabilities

The members of the cardiorenal MDT will be responsible for the policy content, review, and monitoring of compliance. They will ensure the policy complies with national and international guidelines and reflects best evidence-based practice.
All consultants, clinicians, prescribers, pharmacists and nurses should use this guideline and seek advice from a consultant in the cardiorenal MDT if there is any uncertainty regarding how to manage a patient.

3.0 Procedure/Guidelines Detail / Actions

Background

It is estimated that over half of all patients with heart failure (HF) have Chronic Kidney Disease (CKD).
Inhibitors of the renin angiotensin system (RAASi) have significant prognostic benefit in patients with CKD and HF. In addition, mineralocorticoid receptor antagonists (MRAs) and combination RAAS & neprilysin inhibitors (ARNI) also have significant prognostic benefit in HF. Data relevant to each of these indications highlights that the greatest benefit is seen in patients who are able to receive maximal dose of these drugs. Hyperkalaemia limits titration of these treatment options, which can result in suboptimal dosing.
Patiromer and sodium zirconium cyclosilicate (SZC) are both indicated for use in patients with CKD or HF with reduced ejection fraction who cannot tolerate maximal doses of renin-angiotensin system blockade because of persistent serum potassium >5.5mmol/L.
This guidance is designed to define how patiromer and SZC are used chronically to maximise the use of RAASi in patients with CKD or HF where this is limited solely by hyperkalaemia.
This guidance needs to be seen in conjunction with separate guidelines for hyperkalaemia.

Indication

NICE Technology appraisal (TA) guidance published on patiromer and NICE TA guidance published on SZC have made the following recommendations relating to the use of patiromer and SZC for the treatment of hyperkalaemia.
Patiromer or SZC are recommended as an option for treating adults in an in outpatient

setting with persistent hyperkalaemia and chronic kidney disease stage 3b to 5 or heart failure with reduced ejection fraction, if they:
a. have a confirmed serum potassium level of at least 6.0mmol/litre AND
b. are not taking/are not taking an optimised dosage of RAASi because of hyperkalaemia AND
c. are not on dialysis.
This guidance document is aimed at supporting the use of patiromer and SZC in the outpatient environment in order to support the care for people with persistent hyperkalaemia in association with CKD and HF with reduced ejection fraction (HFrEF).

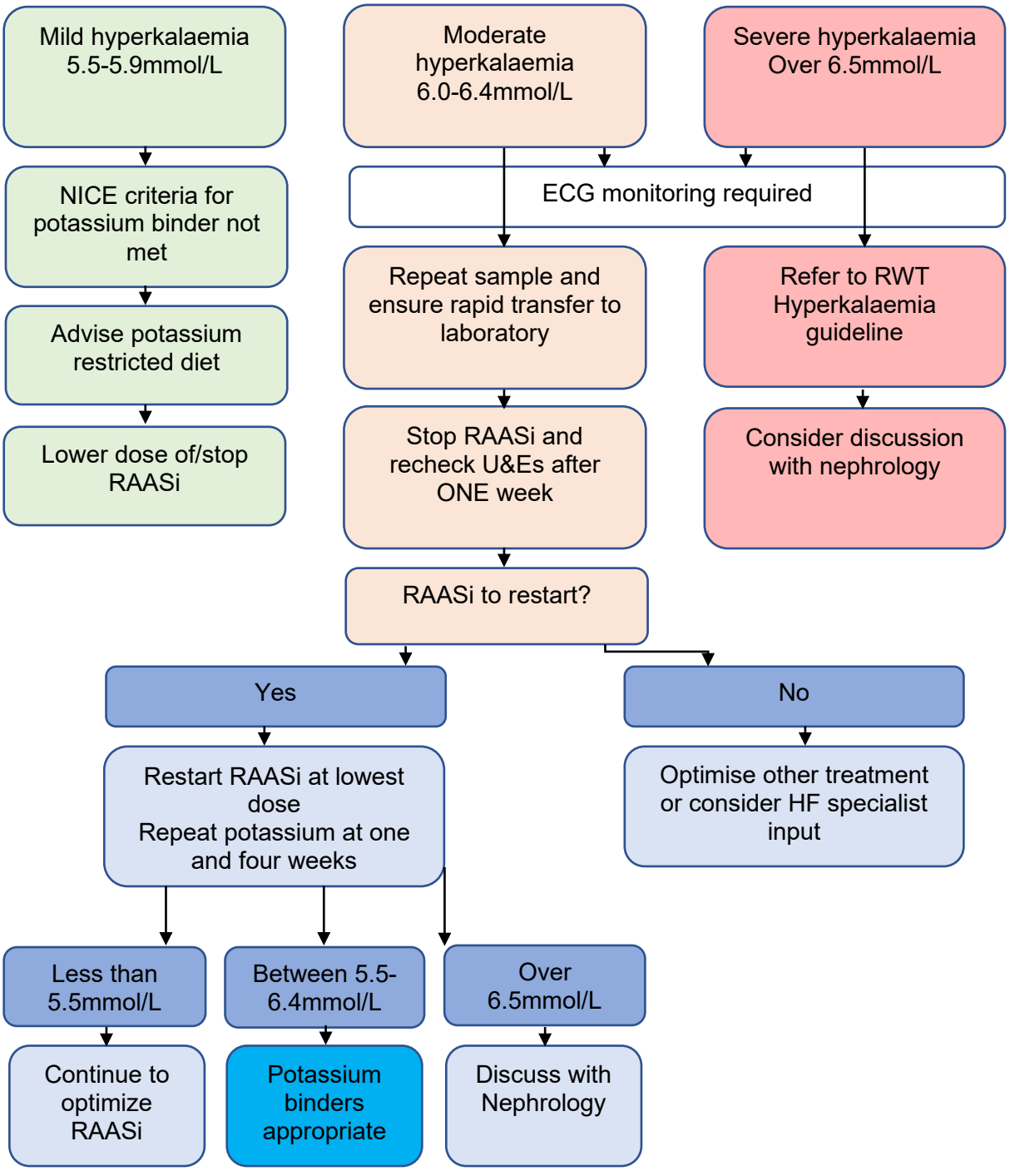
Place in therapy

- Patients with heart failure and hyperkalaemia (potassium 6.0mmol/L or more) should be under review by a HF or Renal specialist.
- Long term use of potassium binders is appropriate for recurrent hyperkalaemia. Typically, these will be patients with previous potassium over 6.0mmol/L whose current potassium is high (greater than 5.5mmol/L) and in whom up-titration of RAASi is planned.
- If hyperkalaemia is secondary to an acute kidney injury (AKI) – consider whether there is an acute trigger. Under these circumstances **hyperkalaemia can be a life-threatening condition and levels greater than 6.0mmol/L should be treated in hospital using RWT Hyperkalaemia Guidelines (available on the Intranet)**

It is important to consider the underlying cause of hyperkalaemia and address as appropriate considering the following:

- Stopping medications that increase potassium for example potassium supplements, potassium retaining laxatives, and trimethoprim; increased dietary potassium intake
- Sampling errors: for example, delays in analysis, taking from drip arm causing pseudohyperkalaemia
- Alternate clinical diagnoses such as adrenal insufficiency

Disclaimer:
Our recommendations are based on current national guidelines and relevant evidence-base. This guideline helps inform clinicians clinical judgement. However, clinicians will consider the trade-off between the benefits and harms of an intervention before making a clinical decision.



Dosing Guidance

<u>Patiromer (Veltassa®)</u>

- Recommended starting dose is 8.4g OD.
- The dose can be increased (or decreased) by 8.4g as needed after a minimum interval of 1 week, based on potassium levels, up to a maximum dose of 25.2g OD.

- Widely available as 8.4g and 16.8g sachets. Note 25.2mg sachets are listed in the summary of product characteristics but they are not currently routinely available.
- Both sachet sizes are equivalent cost therefore to ensure prescribing is cost-effective the prescriber MUST specify the sachet size for 16.8g and 25.2g doses.

Sodium Zirconium Cyclosilicate (Lokelma®)

- Correction phase:
  - The recommended starting dose of SZC is 10 g, administered three times a day for up to 72 hours orally as a suspension in water.
  - When normokalaemia is achieved, the maintenance regimen should be followed.
  - If normokalaemia not achieved after 72 hours consider alternative treatment.

- Maintenance phase:
  - When normokalaemia has been achieved, the minimal effective dose of SZC to prevent recurrence of hyperkalaemia should be established.
  - A starting dose of 5 g once daily is recommended, with possible titration up to 10 g once daily, or down to 5 g once every other day, to maintain a normal potassium level.
  - No more than 10 g once daily should be used for maintenance therapy.

- The 5mg and 10mg sachets are the same cost per gram so there are no cost differences between using ONE x 10g or TWO x 5g sachets.

Choosing between patiromer or SZC

SZC has a slightly more complicated regimen initially due to the acute treatment phase so if compliance is an issue consider patiromer.

If the patient is on multiple medicines throughout the day the correct timing of patiromer may be difficult to achieve as no other medicines should be given 3 hours before or after patiromer. In this event consider SZC.

In patients with a high sodium level, on a restricted sodium intake diet or fluid overloaded patiromer should be considered first line as SZC has a high sodium content.

Patiromer is more prone to inducing gastrointestinal side-effects than SZC therefore patients with GI complaints may fare better with SZC.

Contra-indications

Hypersensitivity to the active substance or any of the excipients

Cautions

Risk factors for hypercalcaemia (calcium partially released from counterion complex) (patiromer)

Contra-indicated if history of bowel obstruction/major GI surgery or swallowing disorder as severe gastro-intestinal disorders (ischaemia, necrosis and intestinal perforation reported with potassium binders)

Low magnesium (patiromer)

Fructose intolerance (contains sorbitol) (patiromer)

Monitoring Requirements

The manufacturers of patiromer advises monitoring serum magnesium at least ONE month after initiation of treatment. If hypomagnesia develops consideration would need to be given to either supplementing the magnesium (refer to Trust Hypomagnesaemia guidelines) or reducing the dose of patiromer depending on the clinicians opinion.

Serum potassium should be monitored ONE to TWO weeks after dose changes or initiating or discontinuing any medications that affect plasma potassium concentration (e.g. potassium binders, RAASi or diuretics).

Potassium binder dose titration		
Serum Potassium	**SZC**	**Patiromer**
Less than 3.5mmol/L	Stop and re-check potassium after ONE week	
3.5-4mmol/L	Decrease dose by 5g/day (minimum dose 5g on alternate days)	Decrease dose by 8.4g/day (minimum dose 8.4g on alternate days)
	Adjust in intervals of ONE week or longer. Discontinue if on lowest dose	
4.0-5.3mmol/L	Continue current dose	
5.4-6.4mmol/L	Increase dose by 5g/day (maximum dose 10g/day)	Increase dose by 8.4g/day (maximum dose 25.2g/day)
	Adjust in intervals of ONE week or longer	
More than 6.5mmol/L	Refer to RWT Hyperkalaemia guideline	

Stop treatment completely, if RAASi therapy is no longer indicated, or if the dose cannot be increased from prior to starting potassium binder.
Reduce dose of RAASi in persistent hyperkalaemia despite optimal doses of potassium binder.
Monitor blood pressure when titrating RAASi therapy.

Patient advice

Sodium Zirconium Cyclosilicate (Lokelma®)

Patients should be advised on how to take SZC.
Manufacturer advises mix the contents of each 5- or 10-g sachet of powder with approximately 45ml of water and stir well. The powder will not dissolve and the suspension should be taken while it is cloudy; if the powder settles it should be stirred again. SZC can be taken with or without food.
Patients should be advised that potential side effects include oedema, constipation and nausea.
Patients should be advised to reduce salt intake (as would be the case for all patients in whom RAASi are indicated) but not to use “lo-salt”
Patients should be advised to seek medical attention if they develop increase swelling of their ankles.
Patients should be advised that SZC may be opaque to X-rays and if undergoing any abdominal x-ray they should let the radiographer know that they are on this drug.
SZC should not be used in women of childbearing age where pregnancy is a possibility
SZC should be taken two hours away from administration of the following medications: azole antifungals (ketoconazole, itraconazole and posaconazole), anti-HIV drugs

(atazanavir, nelfinavir, indinavir, ritonavir, saquinavir, raltegravir, ledipasvir and rilpivirine) and tyrosine kinase inhibitors (erlotinib, dasatinib and nilotinib)

Patiromer (Veltessa®)

Patients should be advised on how to take patiromer according to the following steps:
- The dose should be mixed with approximately 40mLs of water and stirred well. Then add an additional 40mL of water and the suspension should be stirred again thoroughly.
- Apple juice can be substituted for water but this may not be appropriate if the patient has diabetes.
- The powder will not dissolve. More water may be added to the mixture as needed for the patients desired consistency. The mixture should be taken within one hour of initial suspension. If powder remains in the glass after drinking more water should be added and the suspension stirred and taken immediately. This may be repeated as needed to ensure the entire dose is administered.

Administration of patiromer should be separated by at least 3 hours from other oral medications.

Patiromer can be taken with or without food. It should not be heated or microwaved, nor added to heated foods or liquids.
Patiromer should not be taken in its dry form.
Patients should be advised that potential side effects include hypomagnesia, constipation, diarrhoea, abdominal pain, flatulence.
Patiromer should not be used in women of childbearing age where pregnancy is a possibility.

Adherence

Adherence is necessary to prevent hyperkalaemia reoccurring. It is essential to ensure the patient understands that if they stop their potassium binder medication it could lead to their potassium levels becoming dangerously high. If they are thinking of stopping this medication they need to seek medical advice.

Other considerations for raised potassium

If there are alternate reasons for raised potassium, please seek advice from a Nephrologist who contributes to the Heart Failure MDT before initiation to rule out other causes.

4.0 Equipment Required

None required.

5.0 Training

None required. This guideline will be available on the Trust Intranet.

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6.0 Financial Risk Assessment

1	Does the implementation of this document require any additional Capital resources	No
2	Does the implementation of this document require additional revenue resources	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 programs or allocated training times for staff.	No
	Other comments	

7.0 Equality Impact Assessment

Not applicable

8.0 Maintenance

The members of the cardiorenal MDT will ensure the document is reviewed at least every 3 years.

9.0 Communication and Training

This information will be disseminated to all relevant departments.

10.0 Audit Process

Criterion	Lead	Monitoring method	Frequency	Evaluation
100% of patients who have changes made to their therapy in accordance with the guidelines have improved potassium levels	HF cardiologist/nurses	Random audit	Annually	Cardiorenal MDT

11.0 References - Legal, professional or national guidelines

NICE Technology appraisal (TA) guidance published on patiromer on 13th February (https://www.nice.org.uk/ta623)
NICE TA guidance published on SZC on 4th September 2019 (https://nice.org.uk/ta599)

Part A - Document Control

<table>
<tr><td>Procedure/ Guidelines number and version

1.0</td><td>Title of Procedure/Guidelines

The use of potassium binders in the management of persistent hyperkalaemia</td><td colspan="2">Status:

Final</td><td>Author: Principal Pharmacist Renal

Chief Officer Sponsor: Chief Medical Officer</td></tr>
<tr><td rowspan="2">Version / Amendment History</td><td>Version</td><td>Date</td><td>Author</td><td>Reason</td></tr>
<tr><td>1.0</td><td>March 2024</td><td>Principal Pharmacist Renal</td><td>Introduction of guideline</td></tr>
<tr><td colspan="5">Intended Recipients: All medical, nursing and pharmacy staff</td></tr>
<tr><td colspan="5">Consultation Group / Role Titles and Date: Cardiorenal MDT/ cardiologists, nephrologists, heart failure nurses, acute kidney injury nurses, cardiology pharmacists, renal pharmacists 2023
Cardiology Governance – 27/9/23
Renal governance 12/10/23
MMG – 7/11/23</td></tr>
<tr><td colspan="3">Name and date of group where reviewed</td><td colspan="2">Trust Policy Group – March 2024</td></tr>
<tr><td colspan="3">Name and date of final approval committee(if trust-wide document)/ Directorate or other locally approved committee (if local document)</td><td colspan="2">Trust Management Committee – March 2024</td></tr>
<tr><td colspan="3">Date of Procedure/Guidelines issue</td><td colspan="2">March 2024</td></tr>
<tr><td colspan="3">Review Date and Frequency (standard review frequency is 3 yearly unless otherwise indicated – see section 3.8.1 of Attachment 1)</td><td colspan="2">March 2028 every 4 years</td></tr>
<tr><td colspan="5">Training and Dissemination: No training required. Details of new guideline to disseminated via Trust Brief, e-mail information of guideline to key stake holders i.e. clinical directors, matrons</td></tr>
<tr><td colspan="5">To be read in conjunction with: Hyperkalaemia Guideline</td></tr>
<tr><td colspan="5">Initial Equality Impact Assessment: NA</td></tr>
<tr><td colspan="3">Contact for Review</td><td colspan="2">Principal Pharmacist Renal</td></tr>
<tr><td colspan="3">Monitoring arrangements</td><td colspan="2">Cardiorenal MDT; Cardiology Governance Committee</td></tr>
<tr><td colspan="5">Document summary/key issues covered. To advise on the management of hyperkalaemia in patients with cardiorenal syndrome</td></tr>
<tr><td colspan="2">Key words for intranet searching purposes</td><td colspan="3">Cardiorenal; Potassium binder; Patiromer; Veltassa; Sodium Zirconium; Lokelma</td></tr>
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