Optimising RAASi Therapy and Managing Hyperkalaemia in Cardiorenal Disease: A Practical Guide for Healthcare Professionals

This guide is designed to provide healthcare professionals (HCPs) with clear, evidence-based facts and practical strategies, informed by the insights of our Steering Group, for optimising RAASi therapy for long-term cardiorenal protection, along with recommendations for safe and effective use.

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Intended for UK healthcare professionals only.

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*Renin Angiotensin Aldosterone System inhibitor therapy (ACE inhibitors, angiotensin II receptor blockers, angiotensin receptor/neprilysin inhibitor, mineralocorticoid receptor antagonists)

Practical guide to RAASi* optimisation in individuals with cardiorenal disease

Key aims:

1. The prevention and management of hyperkalaemia
2. The optimisation of RAASi therapies for long-term cardiorenal protection

RAASi therapy optimisation describes prescription of RAASi therapy at either:

The highest licensed dose for the indication or the maximal tolerated dose

RAASi therapy optimisation is essential in cardiorenal disease to provide long-term cardiorenal protection

International evidence-based guidelines, for both chronic kidney disease (CKD) and heart failure (HF), recommend treatment with RAASi therapy at target or maximum tolerated doses to achieve the best clinical outcomes[1-3]

In individuals with CKD, RAASi therapies have been evidenced to lower blood pressure and proteinuria, slow the decline of estimated glomerular filtration rate (eGFR) and reduce the risk of end stage kidney disease, cardiovascular (CV) morbidity and all-cause mortality[4,5]

In individuals with HF, RAASi therapies have demonstrated a reduction in CV morbidity and mortality[6]

RAASi therapy optimisation and hyperkalaemia

- ✓ RAASi therapy, in addition to underlying cardiorenal disease, confers an increased risk of hyperkalaemia due to reduced urinary potassium excretion[7,8]
- ✓ **Hyperkalaemia is a predictable, recurrent and manageable risk in individuals on RAASi therapy – requiring a pre-emptive, proactive and long-term approach**
- ✓ **International evidence-based guidelines, for both CKD and HF, emphasise the importance of proactively managing hyperkalaemia to facilitate RAASi therapy optimisation; recommending the use of alternative potassium lowering strategies and therapies, before RAASi therapy down-titration or discontinuation, where clinically appropriate[1-3]**

However...

- ▶ Hyperkalaemia is often managed via the down-titration or discontinuation of RAASi therapy
- ▶ Down-titration or discontinuation of RAASi therapy is associated with increased morbidity and mortality in individuals with cardiorenal disease[9-12]
- ▶ There are alternative potassium lowering strategies and therapies available which can facilitate the continuation and optimisation of RAASi therapy.
  See 'Potassium lowering strategies and therapies'

*Renin Angiotensin Aldosterone System inhibitor therapy (ACE inhibitors, angiotensin II receptor blockers, angiotensin receptor/neprilysin inhibitor, mineralocorticoid receptor antagonists)

How to optimise RAASi therapy in practice

All individuals prior to starting RAASi therapy require thorough assessment:

- ✓ Blood pressure
- ✓ Fluid status
- ✓ Renal function including serum potassium
  - – (CAUTION in starting ACEi/ARB and do not start MRA if potassium >5.0mmol/l[13] seek specialist advice if needed)
- ✓ Concurrent medications
- ✓ Review of risk factors for hyperkalaemia:
  - – Serum potassium
  - – Potassium elevating drugs†
  - – Diet
  - – Poor glycaemic control
  - – Constipation

All individuals must be monitored following initiation and each titration of RAASi therapy dose:

- ✓ Clinical status
- ✓ Renal function:
  - – For ACEi/ARB measure 1-2 weeks after initiation and every dose titration[13]
  - – For MRA measure 1 week after initiation and every dose titration, then monthly for 3 months, then 3-monthly for first year and 4-monthly thereafter[13]
  - – For individuals initiating or titrating haemodynamically active therapies, e.g. RAASi, some eGFR reduction can be expected.1 If serum creatinine rises by >30%, or eGFR falls >25%, this exceeds expected variability and warrants further assessment[14]
  - – Serum potassium – If hyperkalaemia occurs please see **'Practical guide to the definition and management of acute hyperkalaemia in individuals with cardiorenal disease on RAASi therapy' on page 7**

Monitoring after optimisation
Once RAASi therapy dose is established, monitor as per 'Long-term monitoring advice sheet for individuals with cardiorenal disease on RAASi therapy with hyperkalaemia' on page 14.

Potassium lowering strategies and therapies:

1 Address correctable causes of hyperkalaemia:

- ✓ **Adjust potassium elevating drugs†[13] –** Prioritise non-RAASi medications (e.g., NSAIDs, trimethoprim) first, and **down-titrate/discontinue RAASi therapy as a last resort[1]** – see **'RAASi therapy in the context of hyperkalaemia' on page 6**
- ✓ **Modify diet –** Advise a healthy, diverse diet with higher consumption of plant-based foods than animal-based food and low consumption of ultra processed foods.[1] If potassium remains >5.5mmol/l once non-dietary factors are addressed, refer to specialist dietician[13]
- ✓ **Correct metabolic acidosis[13] –** Metabolic acidosis increases risk of hyperkalaemia
- ✓ **Optimise glycaemic control[13] –** Poorly controlled diabetes increases risk of hyperkalaemia
- ✓ **Avoid/address constipation[13] –** Constipation increases the risk of hyperkalaemia

2 Consider potassium lowering medications (acutely or longer term):

- ✓ **Diuretics –** Can increase potassium excretion
- ✓ **Bicarbonate –** Consider adding oral sodium bicarbonate if serum bicarbonate <22mmol/l
- ✓ **Potassium binders –** Remove potassium from the body via the gastrointestinal tract[13]

3 Prevent recurrence of hyperkalaemia:

- ✓ Recurrence of hyperkalaemia should be anticipated and steps taken to avoid it[13]
- ✓ Careful prescribing of potassium elevating drugs – use only where clearly indicated, with particular care if combinations are required, e.g. ACEi/ARB/ARNi + MRA for heart failure (HF)[13]
- ✓ Regular review of correctable causes and consideration of the need for potassium lowering medications (as above)[13] Regular monitoring of bloods (potassium and renal function) and review should occur at the frequency appropriate for the disease state and the individual, e.g. 1-4 times per year for chronic kidney disease (CKD)[1] and HF[2], with additional monitoring during intercurrent illness (especially dehydrating illness), titration of medications that affect potassium levels or renal function, or change in the underlying cardiorenal condition
- ✓ Education of individuals with cardiorenal disease

†Potassium elevating drugs:[13]

- RAASi (ACE inhibitors, angiotensin II receptor blockers, mineralocorticoid receptor antagonists)
- Potassium supplements
- Potassium-sparing diuretics
- Trimethoprim/co-trimoxazole
- Non-steroidal anti-inflammatory drugs
- Non-selective beta-blockers
- Antifungals
- Digoxin
- Salt substitutes
- Herbal medicines (e.g. alfalfa, dandelion)

Sick day guidance – A temporary pause of RAASi therapy, diuretics, metformin and sodium-glucose co-transporter-2 inhibitors during acute dehydrating illness may decrease the risk of acute kidney injury and hyperkalaemia. However, the evidence base for this is weak and there is potential for harm if these medications are not re-instated. **Sick day guidance should be based on an individual risk assessment and there must be a clear plan to re-instate any paused medications.**[1,13]

RAASi therapy in the context of hyperkalaemia:

- Hyperkalaemia associated with RAASi use can often be managed by measures to reduce potassium other than down-titration or discontinuation of RAASi therapy[1]
- Down-titration or discontinuation of RAASi therapies is associated with adverse clinical outcomes in CKD and HF[9-12]
- Only down-titrate or discontinue RAASi as a last resort; if hyperkalaemia is uncontrolled despite **'Potassium lowering strategies and therapies'**, or symptomatic hypotension or serum potassium >6.5mmol/l (until normokalaemia achieved)[1]
- Re-initiate and re-optimise RAASi therapies that are down-titrated or discontinued once normokalaemia is achieved wherever possible – utilise appropriate **'Potassium lowering strategies and therapies' on page 5**
- If hyperkalaemia is preventing RAASi optimisation, seek specialist advice
- N.B. If RAASi therapies are discontinued, also discontinue potassium lowering therapies as appropriate

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Practical guide to the definition and management of acute hyperkalaemia in individuals with cardiorenal disease on RAASi* therapy

Key aims:

1 The prevention and management of hyperkalaemia

2 The optimisation of RAASi therapies for long-term cardiorenal protection

Hyperkalaemia should be considered a predictable, recurrent and manageable issue in individuals with living with cardiorenal disease and treated with RAASi therapy[1]

Assessment†	Mild hyperkalaemia	Moderate hyperkalaemia	Severe hyperkalaemia
Potassium level (mmol/l)[2]	**5.5-5.9**	**6.0-6.4** (address as severe hyperkalaemia if >6.0 with electrocardiogram (ECG) changes)	**>6.5**
Exclude pseudohyperkalaemia[2] (repeat sample in lithium heparin tube) [See Box 1]	Within 3 days if unexpected (otherwise 14 days)	Same day	Urgent hospital assessment
Is the patient acutely unwell? (include consideration of AKI) [See Box 2]	**Yes –** urgent hospital assessment **No –** continue	**Yes –** urgent hospital assessment **No –** continue	Urgent hospital assessment
ECG[2]	**No** ECG required (unless clinical concern)	**Urgent 12 lead ECG** **ECG changes –** urgent hospital assessment [See Box 3] **No ECG changes –** continue	Urgent hospital assessment
Where to assess and manage patient	Community likely appropriate	Same day emergency care via hospital	Urgent hospital assessment

*Renin Angiotensin Aldosterone System inhibitor therapy (ACE inhibitors, angiotensin II receptor blockers, angiotensin receptor/neprilysin inhibitor, mineralocorticoid receptor antagonists)

†Decisions to admit and the route of admission should be based on clinical judgment and local resource, with due consideration of any relevant variables outside of the scope of this guide

Box 1:
Pseudohyperkalaemia[2]
Causes:
Difficult venepuncture, haemolysis, thrombocytosis, erythrocytosis, prolonged or cold storage
Reducing risk:
Label collection time, minimise transit time, optimise storage conditions

Box 2:
Acute Kidney Injury (AKI)
Causes:[3]
- **Prerenal –** reduced blood flow to the kidney, e.g. haemorrhage, diarrhoea and vomiting, cardiogenic shock, nonsteroidal anti-inflammatory drugs (NSAIDs)
- **Renal –** conditions that affect the glomerulus or tubule, e.g. acute tubular necrosis, acute interstitial nephritis
- **Postrenal –** obstructive causes, e.g. renal/ureteric calculi, tumours, enlarged prostate

Diagnosis:[4]
AKI is defined as any of the following:
1. Increase in serum creatinine (sCr) ≥26.5 µmol/L within 48 hours; or
2. Increase in sCr ≥1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or
3. Urine volume <0.5 mL/kg/h for 6 hours

Box 3:
ECG changes associated with hyperkalaemia[2]
Progressive changes:
- Tented T waves
- Prolonged PR interval, flat P waves
- Wide QRS, sine wave, arrythmia, cardiac arrest

Management†

	Mild hyperkalaemia	Moderate hyperkalaemia	Severe hyperkalaemia
Management approach	**If acutely unwell –** urgent hospital assessment **If well –** see **'Potassium lowering strategies and therapies' on page 5**	**If acutely unwell or ECG changes –** urgent hospital assessment **If well –** see **'Potassium lowering strategies and therapies' on page 5**	**Follow local hospital protocol** e.g. UK Kidney Association (UKKA) 5-step approach[2] 1. Protect the heart calcium gluconate, calcium chloride) 2. Shift potassium into cells (insulin dextrose, salbutamol) 3. Remove potassium from the body (potassium binder) 4. Monitor potassium and glucose 5. Prevent recurrence – see **'Potassium lowering strategies and therapies' on page 5**
Approach to RAASi therapy	Continue RAASi therapy if possible – see **'Potassium lowering strategies and therapies'** and **'RAASi therapy in the context of hyperkalaemia' on pages 5 and 6**	Continue RAASi therapy if possible – see **'Potassium lowering strategies and therapies'** and **'RAASi therapy in the context of hyperkalaemia' on pages 5 and 6**	Withold RAASi therapy. Once normokalaemia achieved, re-initiate and re-optimise RAASi therapy if possible. See **'Potassium lowering strategies and therapies' and 'RAASi therapy in the context of hyperkalaemia' on pages 5 and 6**

† Decisions to admit and the route of admission should be based on clinical judgment and local resource, with due consideration of any relevant variables outside of the scope of this guide

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Example hospital discharge summary for an individual with cardiorenal disease on RAASi* therapy with hyperkalaemia

This example document outlines key information and considerations for discharging a patient with cardiorenal disease on RAASi therapy who has hyperkalaemia. It is designed to ensure that follow-up care providers receive comprehensive and relevant details to support optimal patient management.

1 Administration details:

Patient name: Date of birth:

Address:

Postcode:

Admission date: Discharge date: Ward:

Consultant:

Copy summary discharge to: ☐ All treating specialists ☐ GP ☐ Patient

2 Reason for admission: *Hyperkalaemia*

3 Clinical narrative:

Consider:

- *Presentation, e.g. acutely unwell, or hyperkalaemia on routine blood test*
- *Cause of hyperkalaemia*
- *Referrals to secondary care teams Patient information/ education provided status at discharge*
- *Management of hyperkalaemia.*
  Please note:
  - *Correctable causes addressed*
  - *Potassium lowering medications utilised*
  - *Prevention of recurrence plans*
  - *RAASi therapy changes, e.g if down-titrated plans to re-optimise See* ***'Potassium lowering strategies and therapies' and 'RAASi therapy in the context of hyperkaleamia' on pages 5 and 6***

4 Investigations:

Investigation	Results
[Include investigations during admission]	*[Please note salient results underpinning clinical narrative and follow up, e.g. serum potassium levels, renal function]*
[Include planned investigations]	*[Please note timelines and booking status (if requested by secondary care, secondary care are responsible for obtaining results)]*

*Renin Angiotensin Aldosterone System inhibitor therapy (ACE inhibitors, angiotensin II receptor blockers, angiotensin receptor/neprilysin inhibitor, mineralocorticoid receptor antagonists)

5 Medications on discharge:

(State if started during admission)

Medication	Indication	Dose	Planned dose titrations	Intended duration of treatment	Prescribing responsibility

N.B. If starting a medication that primary care are unlikely to be familiar with, consider link to further information, e.g. summary of product characteristics

6 Medications stopped or titrated during admission:

Medication (and indication)	Reason for stopping/titrating	Any further action required

7 Follow up (include timeframes):

Actions for secondary care	Actions for primary care	Actions for patient
Examples…		
✓ *Referrals (ensure secondary care-initiated referrals are completed by secondary care)* ✓ *Clinic review* ✓ *Medication review* ✓ *Blood monitoring*	✓ *Clinic review* ✓ *Medication review* ✓ *Blood monitoring*	✓ *Attendance at appointments* ✓ *Lifestyle/medication compliance* ✓ *Seek help if…*

N.B. Consider the role of primary care as the ongoing management of individuals once they are established on therapy; overseeing those on RAASi therapy and jointly managing those on potassium lowering therapies. The normalisation of potassium levels and the re-introduction and optimisation of RAASi therapy sits with secondary care – **with transfer to primary care once patients are stable.**

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Transfer of care letter for an individual with cardiorenal disease on RAASi* therapy with hyperkalaemia

Dear GP,
Please find below a transfer of care letter from: *[specialist name and speciality]*

1 Patient details:

Name: Date of birth:

Address:

Postcode:

GP details:

Name:

Clinic address:

Postcode:

Specialist details:

Name:

Contact details:

2 Past medical history

Date of diagnosis:

Condition:

[Note cardiorenal diagnoses and all salient health issues]

3 Medication list

Medication:	Indication	Dose	Intended duration

[Note RAASi therapies, potassium lowering therapies, medications that affect renal function or serum potassium, e.g. diuretics, plus all salient medications]

4 Relevant recent results:

Recent examination

Status:

[Note salient, e.g. blood pressure, weight, fluid balance]

Date:

Blood monitoring

Result:

[Note salient, e.g. serum potassium, renal function]

Date:

5 Clinical update:

Example copy: This individual was referred for management of [cardiorenal condition], optimisation of RAASi therapies and normalisation of serum potassium levels.

*Potassium lowering strategies and therapies have been employed (provide details – see **'Potassium lowering strategies and therapies' on page 5.** These should be maintained to prevent recurrence of hyperkalaemia and enable optimisation of RAASi therapy. RAASi therapy has been optimised. This should be maintained for optimal cardiorenal protection see **'RAASi therapy in the context of hyperkalaemia' on page 6.***

Clinical status, serum potassium and medication doses are now stable. Moving forwards, the care of this individual can be appropriately overseen by primary care (may be appropriate if individual on RAASi therapy only), OR jointly managed between primary and secondary care (may be appropriate if individual on potassium lowering therapy in addition to RAASi, or more advanced stages of cardiorenal disease).

6 Suggested roles and responsibilities of primary and secondary care

	Primary care
► **Clinical review**	✓ Usual primary care for underlying condition appropriate to severity (e.g. 1-4 times per year for chronic kidney disease (CKD))[1] ✓ Extra review (if primary care appropriate) at times of intercurrent illness, medication changes or change in underlying condition
► **Medication review**	✓ Review RAASi optimisation and potassium lowering therapies in context of clinical status and blood results
► **Blood monitoring**	✓ Include serum potassium, renal function and any other bloods indicated by medical conditions
► **Prescribing responsibility**	Consider expertise and local area prescribing committee advice: ✓ Primary care to prescribe medications classified as green, e.g. most RAASi therapies ✓ Medications classified as amber, e.g. some potassium lowering therapies, can be prescribed by primary care in conjunction with specialist if sufficient information and support is provided, e.g. shared care agreement ✓ GPs with extended roles in cardiorenal medicine may prescribe more specialist medications

Secondary care	
► **Clinical review**	✓ Usual secondary care for underlying condition appropriate to severity ✓ Extra review (if secondary care appropriate) at times of intercurrent illness, medication changes or change in underlying condition
► **Medication review**	✓ Review RAASi optimisation and potassium lowering therapies in context of clinical status and blood results
► **Blood monitoring**	✓ Routine bloods to be undertaken in primary care ✓ If extra or more specialist tests are deemed appropriate by secondary care, they must be performed, interpreted and actioned by secondary care
► **Prescribing responsibility**	Consider expertise and local area prescribing committee advice: ✓ Secondary care to prescribe medications classified as red, e.g. some potassium lowering therapies ✓ Medications classified as amber, e.g. some potassium lowering therapies, can be prescribed by primary care in conjunction with specialist if sufficient information and support is provided, e.g. via shared care agreement

The next specialist clinic appointment is booked for: *[DD / MM / YYYY]*

OR tick to confirm, **no further specialist appointments have been booked:** ☐

Please contact the department if required for non-urgent concerns with view to advice or re-referral.
For urgent concerns contact the on-call team or send to urgent care or accident and emergency.

Yours sincerely,
[Specialist name and speciality]

References:

1. National Institute For Health and Care Excellence. Evidence review for optimal monitoring frequency in CKD [Internet]. www.nice.org.uk. 2021 Aug. Available from: https://www.nice.org.uk/guidance/ng203/evidence/e-optimal-monitoring-frequency-pdf-9204445986.
2. Alfonzo A, et al. Renal Association Clinical Practice Guidelines: Treatment of Acute Hyperkalaemia in Adults [Internet]. UKKA. 2020 Jul. Available from: chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://ukkidney.org/sites/renal.org/files/RENAL%20ASSOCIATION%20HYPERKALAEMIA%20G UIDELINE%20-%20JULY%202022%20V2_0.pdf
3. Stevens PE, et al. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney International. 2024 Apr 1;105(4):S117–314.
4. McDonagh TA, et al. 2021 ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure. European Heart Journal [Internet]. 2021 Sep 21;42(36):3599–726. Available from: https://academic.oup.com/eurheartj/article/42/36/3599/6358045?login=false
5. Kanda E, et al. Clinical impact of suboptimal RAASi therapy following an episode of hyperkalemia. BMC Nephrology. 2023 Jan 19;24(1).
6. Epstein M, et al. Evaluation of the treatment gap between clinical guidelines and the utilization of renin-angiotensin-aldosterone system inhibitors. The American Journal of Managed Care [Internet]. 2015 Sep 1;21(11 Suppl):S212-220. Available from: https://pubmed.ncbi.nlm.nih.gov/26619183/
7. Linde C, et al. Real-World Associations of Renin–Angiotensin–Aldosterone System Inhibitor Dose, Hyperkalemia, and Adverse Clinical Outcomes in a Cohort of Patients With New-Onset Chronic Kidney Disease or Heart Failure in the United Kingdom. Journal of the American Heart Association [Internet]. 2019 Nov 19;8(22). Available from: https://www.ahajournals.org/doi/10.1161/JAHA.119.012655
8. Leon SJ, et al. Hyperkalemia-Related Discontinuation of Renin-Angiotensin-Aldosterone System Inhibitors and Clinical Outcomes in CKD: A Population-Based Cohort Study. American Journal of Kidney Diseases. 2022 Jan;80(2):164-173.e1.

Long-term monitoring advice sheet for individuals with cardiorenal disease on RAASi* therapy with hyperkalaemia

Key aims:

1 The prevention and management of hyperkalaemia

2 The optimisation of RAASi therapies for long-term cardiorenal protection

All individuals with cardiorenal disease require regular monitoring

- ✓ **Continued optimisation of care**[1]
- ✓ **Detection of progress of disease or co-morbidities**[1]
- ✓ **Discussion of any new advances in care**[1]

Monitoring MUST include

- **Clinical review**, e.g. blood pressure, fluid status, risk prediction tools, symptoms
- **Medication review**, e.g. assess need to start/stop/alter doses, adherence, side effects
- **Blood monitoring**, e.g. potassium and renal function
- **Other relevant investigations**, e.g ECG, echo

Frequency of monitoring

- Frequency of monitoring is determined by the underlying cardiorenal condition and its stage/severity, as well as co-morbidities
- For individuals with co-morbidities, e.g. chronic kidney disease (CKD) and heart failure (HF), take the most conservative (frequent) approach to monitoring

Two specific concerns MUST be addressed at each review

RAASi therapy optimisation:

- Is RAASi therapy optimised for cardiorenal protection?
- If not, why not? Is there a requirement to further optimise?
- Valid reason, e.g. symptomatic hypotension
- Invalid reason, e.g. hyperkalaemia (present or prior – where alternative potassium lowering strategies and therapies have not been instituted)
- See **'RAASi therapy in the context of hyperkalaemia' on page 6**

Hyperkalaemia prevention and management:

- Is hyperkalaemia being proactively prevented and managed?
- See **'Potassium lowering strategies and therapies' on page 5**

*Renin Angiotensin Aldosterone System inhibitor therapy (ACE inhibitors, angiotensin II receptor blockers, angiotensin receptor/neprilysin inhibitor, mineralocorticoid receptor antagonists)

Circumstances requiring additional monitoring[1-3]

Circumstances requiring additional monitoring[1-3]

- ✓ Medication changes – in particular medications that affect potassium levels or renal function, e.g. potassium lowering therapies, RAASi therapies
- ✓ Intercurrent illness – in particular those with the potential to affect renal function or cause acute kidney injury (AKI), e.g sepsis, hypovolaemia
- ✓ Change in the underlying condition(s)

Guidelines for the monitoring of individuals with HF[1,2]

- ► Monitoring should occur at least 6 monthly if the condition is stable
- ► Monitoring requirements increase if the condition is not stable, e.g. from days to weeks

Guidelines for the monitoring of individuals with CKD

✓ Monitoring should occur from 1-4+ times per year, tailored to the underlying cause of CKD, rate of decline of eGFR or increase in albumin creatinine ratio (ACR), plus co-morbidities[5,6]

GFR categories (mL/min/1.73 m²) Description and range			CKD is classified based on: • Cause (C) • GFR (G) • Albuminuria (A)	Albuminuria categories Description and range A1 Normal to mildly increased <30 mg/g <3 mg/mmol	A2 Moderately increased 30–299 mg/g 3–29 mg/mmol	A3 Severely increased ≥300 mg/g ≥30mg/mmol
G1	Normal or high	≥90		Screen 1	Treat 1	Treat 3
G2	Mildly decreased	60-89		Screen 1	Treat 1	Treat 3
G3a	Mildly to moderately decreased	45-59		Treat 1	Treat 2	Treat 3
G3b	Moderately to severely decreased	30-44		Treat 2	Treat 3	Treat 3
G4	Severely decreased	15-29		Treat 3	Treat 3	Treat 4+
G5	Kidney failure	<15		Treat 4+	Treat 4+	Treat 4+

Risk of progression Low risk (if no other markers of kidney disease, no CKD) Moderately increased risk High risk Very high risk

Reproduced from: de Boer IH et al. Kidney Int. 2022;102:974–989.
Notes: Albuminuria and GFR grid reflects the risk of progression by intensity of coloring (green, yellow, orange, red, and deep red). The numbers in the boxes are a guide to the frequency of screening or monitoring (number of times per year).
CKD = chronic kidney disease; GFR = estimated glomerular filtration rate; KDIGO = Kidney Disease: Improving Global Outcomes.
KDIGO CKD Work Group. Kidney Int. 2024;105(4S):S117–S314.

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1. McDonagh TA, et al. 2021 ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure. European Heart Journal [Internet]. 2021 Sep 21;42(36):3599–726. Available from: https://academic.oup.com/eurheartj/article/42/36/3599/6358045?login=false
2. National Institute For Health and Care Excellence. Chronic Heart Failure in adults: Diagnosis and Management [Internet]. www.nice.org.uk. 2018. Available from: https://www.nice.org.uk/guidance/ng106
3. National Institute For Health and Care Excellence. Chronic Kidney Disease: Assessment and Management [Internet]. www.nice.org.uk. 2021. Available from: https://www.nice.org.uk/guidance/ng203
4. Alfonzo A, et al. Renal Association Clinical Practice Guidelines: Treatment of Acute Hyperkalaemia in Adults [Internet]. UKKA. 2020 Jul. Available from: chrome extension://efaidnbmnnnibpcajpcglclefindmkaj/https://ukkidney.org/sites/renal.org/files/RENAL%20ASSOCIATION%20HYPERKALAEMIA%20GUIDELINE%20-%20JULY%202022%20V2_0.pdf
5. Stevens PE, et al. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney International. 2024 Apr 1;105(4):S117–314.
6. Kanda E, et al. Clinical impact of suboptimal RAASi therapy following an episode of hyperkalemia. BMC Nephrology. 2023 Jan 19;24(1).
7. Epstein M, et al. Evaluation of the treatment gap between clinical guidelines and the utilization of renin-angiotensin-aldosterone system inhibitors. The American Journal of Managed Care [Internet]. 2015 Sep 1;21(11 Suppl):S212-220. Available from: https://pubmed.ncbi.nlm.nih.gov/26619183/
8. Linde C, et al. Real-World Associations of Renin–Angiotensin–Aldosterone System Inhibitor Dose, Hyperkalemia, and Adverse Clinical Outcomes in a Cohort of Patients With New-Onset Chronic Kidney Disease or Heart Failure in the United Kingdom. Journal of the American Heart Association [Internet]. 2019 Nov 19;8(22). Available from: https://www.ahajournals.org/doi/10.1161/JAHA.119.012655
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PRESCRIBING INFORMATION

LOKELMA®(sodium zirconium cyclosilicate) 5g & 10g POWDER FOR ORAL SUSPENSION

Consult Summary of Product Characteristics before prescribing.

Indication: Lokelma is indicated for treatment of hyperkalaemia in adults.

Presentation: 5g or 10g powder for oral suspension. Each sachet contains 5g or 10g sodium zirconium cyclosilicate.

Dosage and Administration: **Correction phase:** Recommended starting dose is 10g, administered orally, three times a day as a suspension in water. When normokalaemia is achieved the maintenance regimen should be followed. Typically, normokalaemia is achieved within 24 to 48 hours. If patient is still hyperkalaemic after 48 hours of treatment the same regimen can be continued for an additional 24 hours. If normokalaemia not achieved after 72 hours of treatment, other treatment options should be considered. **Maintenance phase:** Establish the minimal effective dose to prevent recurrence of hyperkalaemia. Recommended starting dose of 5g once daily, with possible titration up to 10g once daily, or down to 5g once every other day, as needed, to maintain normal potassium level. No more than 10g once daily should be used for maintenance therapy. Monitor serum potassium levels regularly during treatment. **Missed dose:** If a dose is missed the patient should take the next usual dose at their normal time. **Renal impairment:** No dosage adjustment required for patients who are not on chronic haemodialysis. For patients on dialysis Lokelma should only be dosed on non-dialysis days. The recommended starting dose is 5g once daily. To establish normokalaemia (4.0-5.0 mmol/L), the dose may be titrated up or down weekly based on the pre-dialysis serum potassium value after the long inter-dialytic interval (LIDI). The dose could be adjusted at intervals of one week in increments of 5g up to 15g once daily on non-dialysis days. It is recommended to monitor serum potassium weekly while the dose is adjusted; once normokalaemia is established, potassium should be monitored regularly (e.g. monthly, or more frequently based on clinical judgement including changes in dietary potassium or medication affecting serum potassium. **Hepatic impairment:** No changes from the normal doses are required for patients with hepatic impairment. **Elderly population:** No special dose and administration guidelines are recommended for this population. **Paediatric population:** Safety and efficacy has not been established in children and adolescents (<18 years). **Method of administration:** The entire contents of the sachet(s) should be emptied in a drinking glass containing approximately 45ml of water and stirred well. The tasteless liquid should be drunk while still cloudy. The powder will not dissolve. If the powder settles, the liquid should be stirred again and taken. If needed, rinse the glass with more water to ensure that all of the content is taken. The suspension can be taken with or without food.

Contraindications: Hypersensitivity to the active substance.

Warnings and Precautions: **Serum potassium levels:** Monitor serum potassium levels when clinically indicated, including after changes are made to medicinal products that affect the serum potassium concentration (e.g. renin-angiotensin-aldosterone system (RAAS) inhibitors or diuretics) and after Lokelma dose is titrated. Monitoring frequency will depend upon a variety of factors including other medicinal products, progression of chronic kidney disease and dietary potassium intake. **Hypokalaemia:** Hypokalaemia may be observed. To prevent moderate to severe hypokalaemia dose titration (maintenance posology) may be required. Discontinue and re-evaluate treatment in patients with severe hypokalaemia. **Worsening of pre-existing heart failure:** Monitor patients with pre-existing heart failure, particularly those in whom an increased sodium intake may lead to fluid overload and decompensation. Manifestations of worsening heart failure, including increased dyspnoea, oedema and rapid weight gain, should be managed as per standard clinical practice. **QT Prolongation:** During correction phase, a lengthening of QT interval can be observed as the physiologic result of decline in serum potassium concentration. **Risk of interaction with X rays:** Sodium zirconium cyclosilicate may be opaque to X-rays, keep in mind if patient has abdominal X-ray. **Intestinal perforation:** Risk of intestinal perforation unknown. Special attention to be paid as intestinal perforation has been reported with potassium binders including Lokelma. **Sodium content:** Lokelma is considered high in sodium. This should be particularly taken into account for those on a low salt diet.

Drug Interactions: No expected effects of other medicines on sodium zirconium cyclosilicate as it is not absorbed or metabolised by the body. Sodium zirconium cyclosilicate can transiently increase gastric pH and can lead to changes in solubility where co-administered medicinal product has pH-dependent stability and therefore should be administered at least 2 hours before or 2 hours after oral medicinal products with clinically meaningful gastric pH dependent bioavailability (e.g. azole antifungals, a number of anti-HIV agents, and tyrosine kinase inhibitors). Sodium zirconium cyclosilicate can be co-administered without spacing of dosing times with oral medicinal products that do not exhibit pH-dependent bioavailability. Tacrolimus should be taken at least 2 hours before or after Lokelma.

Pregnancy and Lactation: Preferable to avoid use during pregnancy. Can be used during breast-feeding.

Ability to Drive and Use Machines: Lokelma has no or negligible influence on the ability to drive and use machines.

Undesirable Events: **Consult SmPC for full list of side effects.** Very Common: Worsening of pre-existing heart failure (including increased dyspnoea, oedema and rapid weight gain). Common: Hypokalaemia, constipation, oedema related events (including fluid retention, generalised oedema, hypervolaemia, localised oedema, oedema, oedema peripheral, peripheral swelling).

Legal Category: POM.

Marketing Authorisation Numbers: PLGB 17901/0332, PLGB 17901/0331.

Presentation & Basic NHS Cost: 5g x 30 pack: £156; 10g x 3 pack: £31.20; 10g x 30 pack: £312.

Business Responsible for Sale and Supply / Further Information: AstraZeneca UK Ltd., 2 Pancras Square, 8th Floor, London, N1C 4AG, UK.

Date of preparation: 02/2026

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Adverse events should be reported.
Reporting forms and information can be found at **www.mhra.gov.uk/yellowcard** or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to AstraZeneca by visiting **https://contactazmedical.astrazeneca.com** or by calling 0800 783 0033.

AstraZeneca