# Practical guidance for the use of potassium binders in the management of hyperkalaemia in patients with heart failure and/or chronic kidney disease

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## Abstract

Given the critical physiological role of potassium, it is understandable that the development of severe hyperkalaemia requires effective management to reduce its effects, which include muscle weakness, paralysis and cardiac arrhythmias. Hyperkalaemia most often results from the failure of renal adaptation to potassium imbalance. Patients who are most susceptible to the development of hyperkalaemia include those with chronic kidney disease and those with heart failure. These patients are often treated with renin–angiotensin–aldosterone system (RAAS) inhibitors, such as angiotensin-converting enzyme inhibitors and angiotensin II-receptor blockers, but the development of hyperkalaemia can require down-titration or cessation of RAAS inhibitors. This presents a significant challenge to nephrologists, cardiologists and healthcare professionals treating these patients as this can prevent them from receiving maximum guideline-directed RAAS inhibitor therapy. Panellists in this roundtable discussion shared their clinical experiences of using potassium binders to manage hyperkalaemia in patients with chronic kidney disease and patients with heart failure (illustrated with case studies) in Northern Ireland and considered recommendations for the implementation and maintenance of chronic potassium-lowering treatment.

Key words: Chronic kidney disease; Heart failure; Hyperkalaemia; Potassium; Potassium binder; Renin–angiotensin–aldosterone system (RAAS) inhibitor

## Introduction

Potassium is the most abundant intracellular cation and plays a key role in the cellular function of nerve and muscle tissue, including maintenance of normal heart rhythm. Dyskalaemias (hypo- or hyperkalaemia) are relatively common in clinical practice and are associated with an increase in all-cause mortality. Mortality risk is lowest with serum potassium values between 4.0 and 5.0 mmol/litre, both in those with and without chronic kidney disease (CKD), heart failure, diabetes mellitus and cardiovascular disease (Collins et al, 2017).

There is no universally agreed upper or lower serum potassium level that defines dyskalaemia. Hypokalaemia occurs when serum potassium drops below the normal range (generally accepted as <3.5 mmol/litre), while hyperkalaemia may be defined as a serum potassium level of above >5.0 mmol/litre (Kovesdy, 2014). A European Cardiology Society expert panel on the management of hyperkalaemia in patients with cardiovascular disease described the severity of hyperkalaemia as mild (serum potassium >5.0 to <5.5 mmol/litre), moderate (serum potassium 5.5–6.0 mmol/litre) or severe (serum potassium 6.0 mmol/litre).

Hyperkalaemia is a serious medical condition that can cause muscle weakness, paralysis and cardiac arrhythmias rarely leading to cardiac arrest and death. Mortality rates in patients with heart failure, hypertension or cardiovascular disease can be as high as 30% (Rosano et al, 2018). Hyperkalaemia most often results from a combination of intrinsic and extrinsic factors (Palmer, 2012; Kovesdy, 2014; Fried et al, 2017). Intrinsic factors include underlying chronic disease, such as chronic kidney disease or heart failure, intercurrent acute diseases such as dehydration and sepsis while common extrinsic factors include drugs that impair physiological responses to raised potassium levels, eg renin–angiotensin–aldosterone

How to cite this article:
Campbell P, McKeveney P, Donegan K, Ataliotis C, Patton C, Mullan R. Practical guidance for the use of potassium binders in the management of hyperkalaemia in patients with heart failure and/or chronic kidney disease. Br J Hosp Med. 2021. https://doi.org/10.12968/hmed.2021.0215

This article is sponsored by Vifor Pharma UK. The content of the article was developed by the authors at a meeting initiated and sponsored by Vifor Pharma. Vifor Pharma reviewed the final version of the article for code compliance and accuracy only. Prescribing information for Veltassa▼ (patiromer) can be found at the end of the article.

Job code UK-PAT-2100045. Date of preparation: April 2021

system (RAAS) inhibitors as well as diets rich in potassium or potassium supplements (Palmer, 2004; Fried et al, 2017). These can all potentially contribute to hyperkalaemia.

The RAAS is a hormonal system that regulates blood pressure and fluid and electrolyte balance including serum potassium levels. Inhibitors of the RAAS include angiotensin-converting enzyme inhibitors (ACEi), angiotensin II-receptor blockers (ARB) and mineralocorticoid receptor antagonists. These drugs are used for the treatment of both chronic kidney disease (CKD) and heart failure as dysfunction in one organ can often induce acute or chronic dysfunction in the other. Decreasing the progression of CKD, via optimising blood pressure control and reducing the occurrence of proteinuria (Gaudreault-Tremblay and Foster, 2020), can therefore help improve outcomes not only for patients with CKD but also for those with heart failure (Ponikowski et al, 2016; Rosano et al, 2018; Renal Association 2020). However, although RAAS inhibitors are established as a cornerstone of the treatment of the cardio-renal syndrome, a key challenge to their use is their association with an increased risk of hyperkalaemia. Discontinuation or down-titration of treatment with RAAS inhibitors can be necessary to avoid hyperkalaemia-related adverse effects (Epstein et al, 2015; Ponikowski et al, 2016; De Fillippis and Desai, 2017; Llubani et al, 2018). However, submaximum treatment with RAAS inhibitors results in worse clinical outcomes in patients with heart failure or CKD than those on the maximum tolerated doses (Epstein et al, 2015). The National Institute for Health and Care Excellence (2014) guidelines for the management of CKD state that treatment with a RAAS inhibitor should not routinely be initiated in patients with CKD with serum K+ >5.0 mmol/litre and, in those receiving RAAS inhibitors, treatment should be discontinued if serum K+ reaches ≥6.0 mmol/litre.

Reducing potassium levels in patients with hyperkalaemia would allow optimisation of guideline-directed medical therapy. A low potassium diet can be a strategy for patients with persistent hyperkalaemia (serum potassium >5.5 mmol/litre) (Renal Association, 2020), although these can be difficult for patients to adhere to while maintaining a balanced diet and/or patients with hypertension who may require a reduced sodium intake (Palmer et al, 2020). Controlling hyperkalaemia by using other drugs in parallel, such as K+ binders, has been shown to allow patients to optimise their RAAS inhibitor therapy and enhance cardiovascular outcomes (Rosano et al, 2018). Two potassium binders are recommended by the National Institute for Health and Care Excellence (2019, 2020): patiromer and sodium zirconium cyclosilicate.

This article summarises the discussion of an expert panel regarding the use of potassium binders in addressing the challenges of hyperkalaemia management in patients with CKD and heart failure.

## Initial and maintenance therapy of hyperkalaemia: current practice in Northern Ireland

In Northern Ireland, the highest population prevalence of CKD (4.3%) is patients at stages 3a (mild to moderate; estimated glomerular filtration rate (eGFR) 45–59 ml/min/1.73m$^2$) and 3b (moderate to severe; eGFR at 30–44 ml/min/1.73m$^2$) (Guidelines and Audit Implementation Network (GAIN), 2015).

Northern Ireland guidelines for the management of CKD (developed by GAIN and the Northern Ireland Nephrology Forum) recommend that in patients with CKD whose serum potassium level is ≥6 mmol/litre, RAAS inhibitors such as angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers are discontinued or their doses downtitrated. Panellists felt that hyperkalaemia prevented them from optimising guideline-directed medical therapy in patients with heart failure, and cardiologists and nephrologists on the panel agreed that K+ binders would be a useful option to help improve treatment with RAAS inhibitors.

The GAIN (2015) guidelines suggest that beginning a low potassium diet and stopping any other medication that could promote hyperkalaemia may allow the reintroduction of RAAS inhibitors for patients who are taking them to treat either heart failure or CKD. It is currently unclear at what serum potassium level K+ binders should be initiated in patients with both conditions, particularly in cases where patients have a potassium level only just below 6.0 mmol/litre.

This article now discusses some case studies outlining management options for patients with hyperkalaemia.

## Patients with heart failure: case 1

A 83-year-old woman was referred to the heart failure service with heart failure with a reduced ejection fraction (left ventricular ejection fraction 35–40%). Her medical history included pre-existing CKD, left bundle–branch block (QRS 120 ms), ischaemic heart disease, hypertension, recent atrial fibrillation and refractory hyperkalaemia (highest level of potassium 7.1 mmol/litre). RAAS inhibitors had previously been stopped or their doses reduced, but this was associated with worsening heart failure symptoms and congestion leading to a hospital admission. Advice on reducing dietary potassium had increased this patient's stress levels because of the conflict between this and advice on healthy eating for cardiovascular disease. The maintenance and up-titration of evidence-based therapy for heart failure was hampered by high potassium levels and impaired renal function. She had been admitted to hospital in October 2019 with hyperkalaemia (potassium 6.4 mmol/litre). She was only taking spironolactone on admission which was stopped on discharge. She was reviewed in the heart failure clinic where she was started on spironolactone 12.5 mg + patiromer 8.4 g once daily. At her next review in the heart failure clinic spironolactone was increased to 25 mg once daily. She missed her next review because of the COVID-19 pandemic.

In November 2020, she was admitted to hospital with breathlessness, orthopnoea and pedal oedema, and she had acute decompensated heart failure. The clinical values on admission were eGFR 25–30 ml/min/1.73m$^2$, sodium 132–139 mmol/litre and potassium 5.4 mmol/litre. She was taking bisoprolol 10 mg/d, spironolactone 25 mg/d as well as apixaban 2.5 mg twice daily, furosemide 40 mg twice daily, isosorbide mononitrate 50 mg, atorvastatin 40 mg and omeprazole 20 mg. She was started on sacubritil/valsartan 24/26 mg twice daily on this admission and continued on patiromer 8.4 g once daily. Her serum potassium has fluctuated between 5.1 and 5.8 mmol/litre. The patient has had no subsequent re-admissions to date for either heart failure decompensation or hyperkalaemia.

The use of patiromer 8.4 g in this patient helped to reduce her hyperkalaemia and allowed the re-introduction of two RAAS inhibitors (spironolactone and sacubritil/valsartan) to improve treatment of heart failure with a reduced ejection fraction.

## Patients with heart failure: case 2

A 67-year-old man with a low ejection fraction had been referred to the heart failure service by the heart failure nursing service as they were unable to maximise guideline-directed medical therapy because of concerns about his estimated glomerular filtration rate and hyperkalaemia. He had a history of hypertension, type 2 diabetes, chronic obstructive pulmonary disease and was an ex-smoker. He had had a myocardial infarction over 20 years ago, and his ejection fraction had been <35% since then. Magnetic resonance imaging showed that the anterior wall was non-viable. He also had chronic kidney disease stage 3B, his estimated glomerular filtration rate had been 38–44 ml/min/1.73m$^2$ for the last 2 years, but had recently declined and was now 30–35 ml/min/1.73m$^2$ with recurrent hyperkalaemia. He was deemed to be on 'optimal medical therapy', and was taking bisoprolol 7.5 mg, eplerenone 12.5 mg once a day, ramipril 2.5 mg, isosorbide mononitrate 25 mg, ivabradine 2.5 mg twice daily, bumetanide 3 mg twice daily and metolazone 2.5 mg once a week. He had previously been on a higher dose of ramipril, but this had been reduced during an admission with acute kidney injury; an attempt to increase the dose 2 years ago had 'failed'. He had previously been on eplerenone 50 mg once a day, but this dose had been reduced and then discontinued over the last year because of recurrent hyperkalaemia.

On arrival at the clinic, his estimated glomerular filtration rate was 39 ml/min/1.73m$^2$, potassium was 5.9 mmol/litre, his systolic blood pressure was 102 mmHg and he had mild volume overload. Dapagliflozin was initiated to treat heart failure with a reduced ejection fraction, and it also reduces the chances of developing moderate–severe hyperkalaemia, particularly while on mineralocorticoid receptor antagonist therapy. At the same time his nitrate and ramipril were discontinued, and he was started on sacubitril/valsartan 24/26 mg twice daily 2 days later, to be reviewed at the outpatient clinic 1 week later with urea and electrolyte measurements. The following week, his estimated glomerular filtration rate was 30 ml/min/1.73m$^2$, K+ 5.7 mmol/litre, his jugular venous pressure was 10 cm$H_2O$ and he had no adverse side effects. At clinic the following week his urea and electrolytes were stable, his jugular venous pressure was 8 cm$H_2O$ and his systolic blood pressure was 108 mmHg. Sacubitril/valsartan was uptitrated to 49/51 mg twice daily, and bumetanide was reduced to 3 mg at 8am and 2 mg at 2pm. At clinic 2 weeks later his estimated glomerular filtration rate was 31 ml/min/1.73m$^2$, K+ 5.7 mmol/litre, jugular venous pressure low, systolic blood pressure was 96 mmHg and he was a little dizzy. His dose of bumetanide was further reduced to 1 mg twice daily. At clinic review a further 2 weeks later, his estimated glomerular filtration rate was 33 ml/min/1.73m$^2$, K+ 5.6 mmol/litre, systolic blood pressure 104 mmHg, jugular venous pressure 7 cmH2O. His sacubitril/valsartan was increased to 97/103 mg twice daily and dapagliflozin 10 mg once daily was added. One week after his last dose increase, his estimated glomerular filtration rate was 34 ml/min/1.73m$^2$ and K+ 5.5 mmol/litre.

At the initiation of the care plan, discussion was held between the cardiology and renal team at the cardiorenal multidisciplinary team meeting, to determine if the patient, with potassium levels around 5.8 mmol/litre, should commence a potassium binder, so as to enable use of maximal guideline-directed medical therapy for heart failure with a reduced ejection fraction.

### Patients with chronic kidney disease: case 3

An 84-year-old female inpatient (body mass index 38.5 kg/m$^2$) with stable CKD 4/5 and cystinuria with multiple staghorn calculi, was treated with bumetanide 1 mg/d. The patient's previous medical history included gout, ischaemic heart disease with ST-segment elevation myocardial infarction, reduced left ventricular function, hypertension and pulmonary embolism. She had a fibula fracture, urinary tract infection, acute kidney injury and an asymptomatic confirmed peak K+ level of 6.2 mmol/litre associated with a stable eGFR (16 ml/min/1.73m$^2$), so she was initiated on patiromer 8.4 g per day for 9 days.

Her treatment objectives were achieved, lowering her serum K+ level to 4.2 mmol/litre with no changes noticed in the high range levels of creatinine (207–240 µmol/litre) or urea (15.6–26.9 mmol/litre). Serum magnesium concentration remained within the normal range (at 0.93 mmol/litre) for 1 month of treatment with patiromer and calcium was stable at 2.47 mmol/litre.

### Patients with chronic kidney disease: case 4

An 87-year-old female inpatient with advanced CKD (diagnosed 7 years ago) and recently diagnosed heart failure with preserved ejection fraction (left ventricular ejection fraction 45–49%) presented with clinical symptoms of fatigue. She was frail and her medical history included hypertension, ischaemic heart disease, cerebrovascular accident, myelodysplasia (treated with high dose erythropoietin) and mild/moderate coeliac disease. With no RAAS inhibitor therapy, she had bumetanide 1 mg three times a week and was started on sodium bicarbonate 1 g twice a day for metabolic acidosis.

Her end-stage renal disease (eGFR of 9 ml/min/1.73m$^2$) was being managed conservatively. Patiromer 8.4 g/d was initiated to treat a confirmed peak serum K+ of 6.4 mmol/litre. On day 3 after starting patiromer, her serum K+ level dropped to 4.3 mmol/litre and remained at this level for 5 more days. Serum creatinine (307–385 mmol/litre) and urea (22.4–43.3 mmol/litre) fluctuated with adjustments to diuretic therapy during the admission.

After 1 month's treatment with patiromer, the patient had a normal stable calcium level (2.46 mmol/litre) and a reduced stable magnesium level (0.67 mmol/litre), and potassium remained in the normal range.

## Management of acute and chronic hyperkalaemia

### Acute hyperkalaemia

Acute hyperkalaemia can be defined as a sudden, rapid increase in serum potassium levels. The response to hyperkalaemia is guided by its severity (serum potassium level) and electrocardiographic changes. A serum potassium level greater than 6.5 mmol/litre with electrocardiographic changes is considered a life-threatening emergency with an increased risk of cardiac toxicity and arrhythmia, and should be treated accordingly (Renal Association, 2020). The basic pathophysiology of hyperkalaemia involves either an intracellular to extracellular potassium shift or decreased renal excretion. Cellular injury can release large quantities of intracellular potassium into the extracellular space (Mushiyakh et al, 2012). There can be a number of causes including rhabdomyolysis from a crush injury, excessive exercise, metabolic acidosis or other haemolytic processes, although these tend to be transient unless concomitant renal pathology is present. Clinical studies are supported by UK guidance on the management of acute hyperkalaemia (Elliott et al, 2010; Renal Association, 2020). Figure 1 demonstrates the treatment options for patients with acute hyperkalaemia when it occurs in an emergency setting.

Emergency treatment is performed in a step-wise manner, requiring membrane stabilisation (calcium salts), then potassium redistribution (β adrenergic agonists, insulin, sodium bicarbonate) to help avoid cardiac arrhythmias followed by elimination of K+ using dialysis, loop diuretics or K+ binders (Clase et al, 2020; Renal Association, 2020) (Figure 1). More recently available potassium binders such as patiromer or sodium zirconium cyclosilicate may be used instead of the older cation exchange resins, sodium polystyrene sulfonate (SPS) or calcium polystyrene sulfonate (CPS) to remove potassium. These resins lower K+ levels in the acute setting, but their transient effect on serum K+ levels, limited long-term data, issues with tolerance specifically the risk of serious gastrointestinal adverse effects (including life-threatening intestinal necrosis) and sodium load precautions (with SPS) limit their use for the management of chronic hyperkalaemia (Electronic Medicines Compendium, 2020, 2021; Renal Association, 2020).

## Chronic hyperkalaemia

Chronic or persistent hyperkalaemia is caused by the impairment of potassium excretory processes and/or increased potassium load and often requires ongoing management. Figure 2 demonstrates the treatment options for patients with chronic hyperkalaemia. Management of chronic hyperkalaemia in patients with CKD and/or heart failure remains a challenge and is associated with a number of comorbidities (De Nicola et al, 2018).

In recent years, the K+ binders patiromer and sodium zirconium cyclosilicate have been introduced for the treatment of hyperkalaemia in adults.

Patiromer is a non-specific organic ion-exchange resin, where calcium exchanges for potassium. Patiromer increases faecal potassium excretion through binding of potassium in the lumen of the gastrointestinal tract. Binding of potassium reduces the concentration of free potassium in the gastrointestinal lumen, resulting in a reduction of serum potassium levels (Electronic Medicines Compendium, 2020).

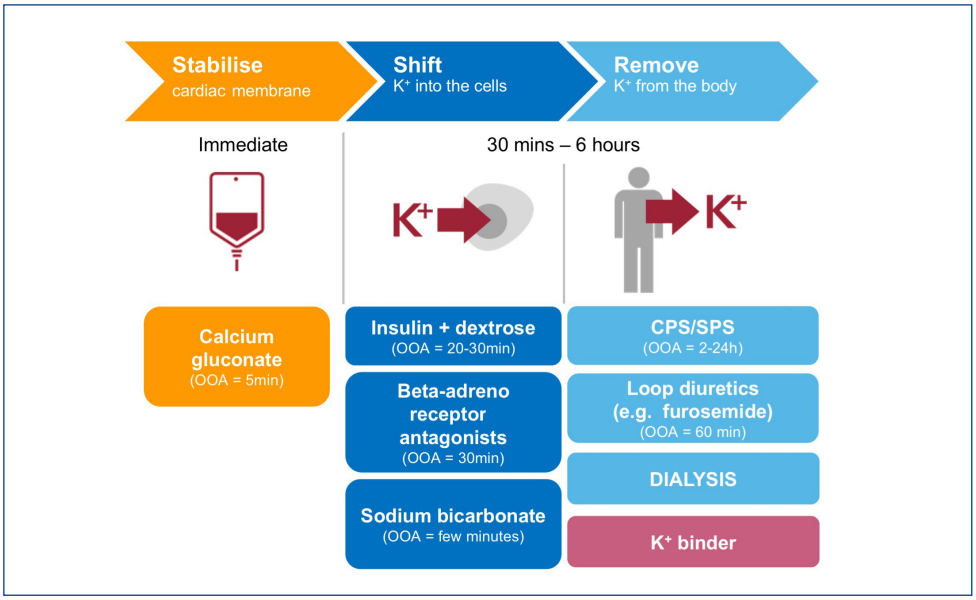


**Figure 1.** Management of acute hyperkalaemia. CPS = calcium polystyrene sulfonate; OOA = onset of action; SPS = sodium polystyrene sulfonate. From Weisberg (2008), Raebel (2012), Electronic Medicines Compendium (2020, 2021).

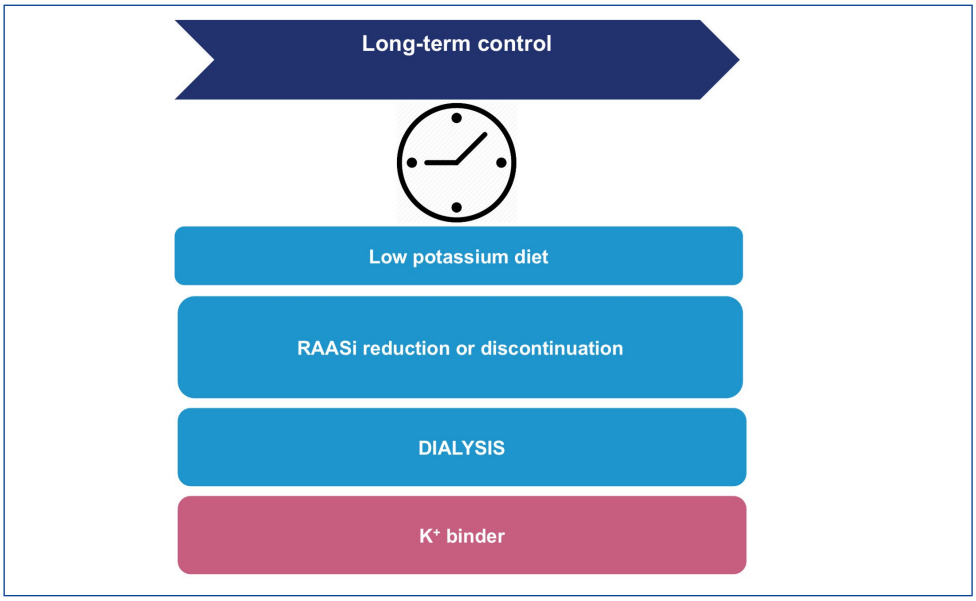


**Figure 2.** Management of chronic hyperkalaemia. RAASi = renin–angiotensin–aldosterone system inhibitor. From De Nicola et al (2018), Electronic Medicines Compendium (2020, 2021).

Pooled safety and efficacy analysis of patiromer for the management of hyperkalaemic patients, from three clinical trials demonstrated that this drug is well tolerated and able to significantly reduce serum K+ levels (Pitt et al, 2011; Bakris et al, 2015; Weir et al, 2015). The majority of adverse reactions reported from trials were mild to moderate gastrointestinal disorders (most common: constipation (6.2%), diarrhoea (3%), abdominal pain (2.9%), flatulence (1.8%)). These were generally mild to moderate and not dose related. Mild to moderate hypomagnesaemia (5.3%) was also reported (no patient developed a serum magnesium level <1 mg/dl (0.4 mmol/litre); Electronic Medicines Compendium, 2020).

Sodium zirconium cyclosilicate is a non-absorbed, non-polymer inorganic powder that captures potassium in exchange for hydrogen and sodium cations. Sodium zirconium cyclosilicate captures potassium throughout the entire gastrointestinal tract and reduces the concentration of free potassium in the gastrointestinal lumen, thereby lowering serum potassium levels and increasing faecal potassium excretion to resolve hyperkalaemia (Electronic Medicines Compendium, 2021).

The potassium-lowering effects of sodium zirconium cyclosilicate have been demonstrated in three randomised, double-blind, placebo-controlled trials in patients with hyperkalaemia. Of patients taking sodium zirconium cyclosilicate, 4.1% developed hypokalaemia (serum potassium <3.5 mmol/litre), which was resolved with dose adjustment or discontinuation of sodium zirconium cyclosilicate. Oedema-related events were reported by 5.7% of patients taking sodium zirconium cyclosilicate, including fluid overload, fluid retention, generalised oedema, hypervolaemia, localised oedema, and peripheral swelling (Electronic Medicines Compendium, 2021).

National Institute for Health and Care Excellence (2019, 2020) recommend that these potassium binders can be used under the following circumstances:

- in emergency care for acute life-threatening hyperkalaemia alongside standard care
- for people with persistent hyperkalaemia and stages 3b–5 chronic kidney disease or heart failure, if they:
  - have a confirmed serum potassium level of at least 6.0 mmol/litre and
  - are not taking, or are taking a reduced dosage of, a RAAS inhibitor because of hyperkalaemia
  - are not on dialysis.

## Panellists' recommendations for treatment of hyperkalaemia

The panellists' discussion took into consideration national guidance on the management of hyperkalaemia. The outcome is summarised in Table 1:

**Table 1. Use of potassium binders to treat hyperkalaemia**

| | |
|---|---|
| Treating hyperkalaemia | Patiromer and sodium zirconium cyclosilicate have a potential role in managing both acute and chronic hyperkalaemia |
| | Patients and clinicians are keen for treatment options that would allow them to continue using RAAS inhibitors at their optimal guideline-recommended dose |
| | It is important to balance the risk with benefit of continuing long-term RAAS inhibitor therapy |
| | Although it is not intended that potassium binders replace a low-potassium diet, they may help to mitigate the impact of such a diet on overall nutrition |
| Clinical effectiveness | More recent potassium binders may be useful as a potential option for delaying or avoiding the initiation of acute dialysis, or as an alternative to diuretics and calcium polystyrene sulfonate or sodium polystyrene sulfonate for treating hyperkalaemia, alongside standard care |
| | The panellists agreed with the National Institute for Health and Care Excellence (2019, 2020) technology appraisals that use of potassium binders could avoid the need to stop RAAS inhibitors if the patient's serum potassium level reaches 6 mmol/litre to decrease mortality, hospitalisation and disease progression |

*With reference to National Institute for Health and Care Excellence (2019) Technology appraisal guidance [TA599] and National Institute for Health and Care Excellence (2020) Technology appraisal guidance [TA623]. RAAS = renin–angiotensin–aldosterone system.*

## Implementation and use of potassium binders: practical solutions

National Institute for Health and Care Excellence's (2019, 2020) technology appraisals support the use of patiromer or sodium zirconium cyclosilicate to enable RAAS inhibitor optimisation and thus slow the progression of CKD and/or help manage symptomatic heart failure. While National Institute for Health and Care Excellence (2019, 2020) recommends that patiromer or sodium zirconium cyclosilicate should be given to patients with persistent hyperkalaemia whose serum K+ >6 mmol/litre, some clinicians may initiate K+ binder therapy at serum K+ levels of 5.8 mmol/litre.

There is no agreed protocol for the initiation and use of K+ binders in Northern Ireland. However, the Northern Ireland Kidney research fund are supporting two research projects on 'increased risk for heart disease in persons with chronic kidney disease' and 'reasons for

**Table 2. A guide for initiating and continuing potassium binders in appropriate patients with CKD and/or heart failure**

| | | |
|---|---|---|
| Identification | Who is at risk of hyperkalaemia? | Patients with CKD and/or heart failure |
| | | Patients who are on treatment with RAAS inhibitors |
| | | Patients with diabetes |
| | | Patients with hypoadrenalism (also known as those with Addison's disease) |
| | | Patients who present acutely with dehydration, ischaemia, hypoxic injury (as a result of respiratory failure), burns or acute kidney injury |
| | Note: Patients who present with a rapid rise in serum potassium accompanied by electrocardiographic changes should be treated as an emergency | |
| | Who should be identifying these patients? | In addition to the consultant nephrologist or cardiologist, healthcare professionals who treat patients with heart failure or CKD, such as a diabetes nurse specialist, junior doctor, trauma staff or consultant pharmacist, should be able to perform this identification step. These will typically take place in heart failure, diabetic or vascular clinics, acute medical and inpatient cardiology, emergency departments or primary care |
| Initiation of potassium binders | The decision to start a patient with persistent or chronic hyperkalaemia on potassium binders should be taken during a multidisciplinary team discussion. The panel agreed that, currently, eligible patients should be initiated on potassium binders by a cardiologist or a renal physician in secondary care only. However, the panel suggested that in future this could be done by a specialist nurse or in the primary care setting by a GP. In all cases, this should be communicated to the patient's GP. Primary care prescribing would be dependent on increased awareness of and education regarding potassium binders and the importance of controlling potassium levels. The panel strongly believed that appropriate use of potassium binders would reduce hospital admissions and costs related to hyperkalaemia. However, specific regional or national guidelines for primary care teams would be needed to help prescribe potassium binders appropriately | |
| Monitoring patients who have been started on potassium binders | If patients are started on or have changes to treatment that could impact their potassium levels (e.g. RAAS inhibitor or potassium binder), urea and electrolytes (U&E) should be checked within 1–2 weeks<br>The panel suggested that monitoring could be done by the initiating consultant, specialist nurses or consultant pharmacists, although specific regional or national guidelines for primary care teams would be needed to guide the monitoring of patients who are taking potassium binders. Patients should be advised that they will be required to come back for a blood test to check their U&Es within the first 2 weeks of initiation | |
| Review | Review could be carried out either by the same clinician conducting the regular monitoring or a nurse specialist. Frequency of review will depend on the patient's clinical status, for example U&E results, blood pressure control and kidney function. The daily dose of potassium binders should be adjusted in accordance with their prescribing information in order to achieve the desired target serum potassium level | |
| Transfer of care | The panel agreed that, in addition to potassium levels remaining within agreed parameters, any transfer of care from secondary to primary for patients treated with a potassium binder would depend on consistent, effective communication between primary care and secondary care. Any acute decline of renal function or potassium levels persistently above agreed targets will require transfer back to the secondary team, while those with a stable K+ level between 4.5 and 5 mmol/litre could remain under community care | |

## Key points

- Hyperkalaemia is relatively common in clinical practice and is associated with an increase in all-cause mortality.
- Renin–angiotensin–aldosterone system (RAAS) inhibitors remain the cornerstone treatment of patients with chronic kidney disease and heart failure, but are associated with raised potassium levels.
- Non-initiation, reduction or discontinuation of RAAS inhibitors, because of the risk of the patient developing hyperkalaemia, can result in suboptimal management of patients with chronic kidney disease and/or heart failure.
- Potassium binders provide another option to maintain optimum RAAS inhibitor therapy alongside standard care in patients with chronic kidney disease or heart failure, to help slow progression of chronic kidney disease and cardiovascular complications.
- A more structured approach, involving the wider multidisciplinary team, may help healthcare professionals identify and treat patients with hyperkalaemia.

rapid weight loss in dialysis patients' (Maxwell, 2019) which may provide more evidence to inform future practice. During the meeting, panellists discussed the Renal Association (2020) algorithm for managing hyperkalaemia in the chronic setting, and agreed the optimal approach for managing patients with chronic hyperkalaemia (Table 2).

Panellists gave the following recommendations to help support primary care physicians and optimise the initiation, adherence and maintenance of potassium binders.

- Heart failure/CKD management: the importance of optimisation and achieving guideline recommended dosing of medication
- Initiation of potassium binders should be considered for hyperkalaemic patients with serum K+ ≥6 mmol/litre to facilitate uptitration of RAAS inhibitor therapy that would otherwise be downtitrated or even discontinued
- Experience sharing: encourage sharing of clinical experience of using potassium binders
- Diagnosis and monitoring: implementation of a rapid assessment service to review clinical status and medications. A consultant or community pharmacist could review management of hyperkalaemia where appropriate. This would be dependent on the local service, but specific regional or national guidelines would be needed to guide the monitoring of patients who are taking potassium binders
- Ongoing education: encouraging primary care teams to keep up to date on latest management strategies and guideline revisions on the management of hyperkalaemia, for example identifying patients in the community at risk of developing hyperkalaemia, optimising RAAS inhibitor therapy.
- Optimising patient medication adherence: primary care physicians should provide patients with a clear explanation of how potassium binders work, how they should be initiated and where they fit with their CKD and heart failure medications plus an awareness of additional available support from specialist nurses

The implementation and maintenance of potassium binders should be encouraged to permit optimal use of RAAS inhibitor therapies, to help achieve serum potassium targets in patients with hyperkalaemia. This may help manage dietary restrictions and the need for dialysis in patients with CKD and/or heart failure.

## Conclusions

Patients who are most susceptible to the development of hyperkalaemia include those with CKD and those with heart failure. The benefits of treating these patients with RAAS inhibitors are clear, but non-initiation, reduction or discontinuation of RAAS inhibitors, because of the risk of the patient developing hyperkalaemia, can result in suboptimal management of patients with CKD and/or heart failure. However, the newer classes of heart failure medications, such as sodium-glucose co-transporter-2 inhibitors and angiotensin receptor-neprilysin inhibitors, may have less of an impact on potassium levels.

The more recently available potassium binders provide a promising method to control hyperkalaemia in the chronic setting by allowing patients to continue on their optimum RAAS inhibitor therapy. In addition, they allow effective control of elevated serum K+ level, alongside standard care, in the acute and/or emergency settings. A more structured approach, involving the wider multidisciplinary team, may help healthcare professionals identify and treat patients with hyperkalaemia.

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**Conflicts of interest**

All panellists except Carol Patton received an honorarium for participating in the roundtable discussion. Carol Patton, Kay Donegan, Paul McKeveney and Charlie Ataliotis declare no conflicts of interest; Robert Mullan has received honoraria from Vifor Pharma for participating in advisory boards; Patricia Campbell has received speaker fees from Novartis, Vifor, Pfizer and Boehringer Ingelheim..

## References

Bakris GL, Pitt B, Weir MR et al. Effect of patiromer on serum potassium level in patients with hyperkalemia and diabetic kidney disease: The AMETHYST-DN Randomized Clinical Trial. JAMA. 2015;314(2):151–161. https://doi.org/10.1001/jama.2015.7446

Clase CM, Carrero JJ, Ellison DH et al; Conference Participants. Potassium homeostasis and management of dyskalemia in kidney diseases: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney Int. 2020;97(1):42–61. https://doi.org/10.1016/j.kint.2019.09.018

Collins AJ, Pitt B, Reaven N et al. Association of serum potassium with all-cause mortality in patients with and without heart failure, chronic kidney disease, and/or diabetes. Am J Nephrol. 2017;46(3):213–221. https://doi.org/10.1159/000479802

De Nicola L, Di Lullo L, Paoletti E, Cupisti A, Bianchi S. Chronic hyperkalemia in non-dialysis CKD: controversial issues in nephrology practice. J Nephrol. 2018;31(5):653–664. https://doi.org/10.1007/s40620-018-0502-6

Elliott MJ, Ronksley PE, Clase CM, Ahmed SB, Hemmelgarn BR. Management of patients with acute hyperkalemia. CMAJ. 2010;182(15):1631–1635. https://doi.org/10.1503/cmaj.100461

Electronic Medicines Compendium. Resonium A. 2019a. https://www.medicines.org.uk/emc/product/1461 (accessed 5 February 2021)

Electronic Medicines Compendium. Calcium Resonium 99.934% w/w Powder for Oral/Rectal Suspension. 2019b. https://www.medicines.org.uk/emc/product/1439 (accessed 5 February 2021)

Electronic Medicines Compendium. Veltassa (Patiromer) 8.4 g powder for oral suspension. 2020. https://www.medicines.org.uk/emc/product/779/smpc (accessed 5 February 2021)

Electronic Medicines Compendium. Lokelma 5 g powder for oral suspension. 2021. https://www.medicines.org.uk/emc/product/10059/smpc (accessed 18 February 2021)

Epstein M, Reaven NL, Funk SE, McGaughey KJ, Oestreicher N, Knispel J. Evaluation of the treatment gap between clinical guidelines and the utilization of renin-angiotensin-aldosterone system inhibitors. Am J Manag Care. 2015;21(11 Suppl):S212-20

Fried L, Kovesdy CP, Palmer BF. New options for the management of chronic hyperkalemia. Kidney Int Suppl (2011). 2017;7(3):164–170. https://doi.org/10.1016/j.kisu.2017.09.001

Gaudreault-Tremblay MM, Foster BJ. Benefits of continuing RAAS inhibitors in advanced CKD. Clin J Am Soc Nephrol. 2020;15(5):592–593. https://doi.org/10.2215/CJN.02920320

Guidelines and Audit Implementation Network. Northern Ireland Guidelines for the Management of Chronic Kidney Disease (CKD). Practical Points for Use of Estimated GFR and Albuminuria

(ACR) in Assessing CKD. 2015. https://www.rqia.org.uk/RQIA/files/41/4125a465-346c-4f4f-a8c6-5e534e6d1b2d.pdf (accessed 15 January 2021)

Kovesdy CP. Management of hyperkalaemia in chronic kidney disease. Nat Rev Nephrol. 2014;10(11):653–662. https://doi.org/10.1038/nrneph.2014.168

Llubani R, Vukadinović D, Werner C, Marx N, Zewinger S, Böhm M. Hyperkalaemia in heart failure-pathophysiology, implications and therapeutic perspectives. Curr Heart Fail Rep. 2018;15(6):390–397. https://doi.org/10.1007/s11897-018-0413-9

Maxwell P. Research into Chronic kidney disease. 2019. https://www.kidneyresearchni.com/how-we-help/research (accessed 15 January 2021)

Mushiyakh Y, Dangaria H, Qavi S, Ali N, Pannone J, Tompkins D. Treatment and pathogenesis of acute hyperkalemia. J Community Hosp Intern Med Perspect. 2012;1(4):10.3402/jchimp.v1i4.7372. https://doi.org/10.3402/jchimp.v1i4.7372

National Institute for Health and Care Excellence. Chronic kidney disease in adults: assessment and management. 2014. https://www.nice.org.uk/guidance/cg182/resources/chronic-kidney-disease-in-adults-assessment-and-management-pdf-35109809343205 (accessed 15 January 2021)

National Institute for Health and Care Excellence. Sodium zirconium cyclosilicate for treating hyperkalaemia. 2019. https://www.nice.org.uk/guidance/ta599/resources/sodium-zirconium-cyclosilicate-for-treating-hyperkalaemia-pdf-82607272135621 (accessed 4 February 2021)

National Institute for Health and Care Excellence. Patiromer for treating hyperkalaemia. 2020. https://www.nice.org.uk/guidance/ta623/resources/patiromer-for-treating-hyperkalaemia-pdf-82609015577029 (accessed 15 January 2021)

Palmer BF. Managing hyperkalemia caused by inhibitors of the renin–angiotensin–aldosterone system. N Engl J Med. 2004;351(6):585–592. https://doi.org/10.1056/NEJMra035279

Palmer BF. Hyperkalemia in predialysis patients. Clin J Am Soc Nephrol. 2012;7(8):1201–1202. https://doi.org/10.2215/CJN.06060612

Palmer BF, Carrero JJ, Clegg DJ et al. Clinical management of hyperkalemia. Mayo Clin Proc. 2020:S0025-6196(20)30618-2. https://doi.org/10.1016/j.mayocp.2020.06.014

Pitt B, Anker SD, Bushinsky DA, Kitzman DW, Zannad F, Huang IZ; PEARL-HF Investigators. Evaluation of the efficacy and safety of RLY5016, a polymeric potassium binder, in a double-blind, placebo-controlled study in patients with chronic heart failure (the PEARL-HF) trial. Eur Heart J. 2011;32(7):820–828. https://doi.org/10.1093/eurheartj/ehq502

Ponikowski P, Voors AA, Anker SD et al; ESC Scientific Document Group. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J. 2016;37(27):2129–2200. https://doi.org/10.1093/eurheartj/ehw128

Raebel MA. Hyperkalemia associated with use of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers. Cardiovasc Ther. 2012;30(3):e156–66. https://doi.org/10.1111/j.1755-5922.2010.00258.x

Renal Association. Treatment of Acute Hyperkalaemia in Adults. 2020. https://renal.org/sites/renal.org/files/RENAL%20ASSOCIATION%20HYPERKALAEMIA%20GUIDELINE%202020.pdf (accessed 15 January 2021)

Rosano GMC, Tamargo J, Kjeldsen KP et al. Expert consensus document on the management of hyperkalaemia in patients with cardiovascular disease treated with renin angiotensin aldosterone system inhibitors: coordinated by the Working Group on Cardiovascular Pharmacotherapy of the European Society of Cardiology. Eur Heart J Cardiovasc Pharmacother. 2018;4(3):180–188. https://doi.org/10.1093/ehjcvp/pvy015

Weir MR, Bakris GL, Bushinsky DA et al; OPAL-HK Investigators. Patiromer in patients with kidney disease and hyperkalemia receiving RAAS inhibitors. N Engl J Med. 2015;372(3):211–221. https://doi.org/10.1056/NEJMoa1410853

Weisberg LS. Management of severe hyperkalemia. Crit Care Med. 2008;36(12):3246–3251. https://doi.org/10.1097/CCM.0b013e31818f222b

# Veltassa® ▼(patiromer sorbitex calcium)

**Prescribing Information - UK**

**For full prescribing information refer to the Summary of Product Characteristics (SmPC)**

**Active ingredient:** patiromer sorbitex calcium
**Presentation** Powder for oral suspension available in sachets containing either 8.4g,16.8g.
**Indication:** Treatment of hyperkalaemia in adults.
**Dosage and Administration:** The recommended starting dose is 8.4 g administered orally once daily with or without food. The daily dose may be adjusted by 8.4 g as needed at one-week intervals or longer to reach desired serum potassium target range, up to a maximum dose of 25.2 g daily. If serum potassium falls below the desired range, the dose should be reduced or discontinued. If a dose is missed, the missed dose should be taken as soon as possible on the same day and should not be taken with the next dose. Administration of Veltassa should be separated by 3 hours from other oral medicinal products. The onset of action occurs 4–7 hours after administration. Veltassa should not replace emergency treatment for life-threatening hyperkalaemia. There is limited data on the use of Veltassa in patients on dialysis; no special dose and administration guidelines were applied to these patients in clinical studies.The complete dose should be poured into a glass containing approximately 40ml of water, then stirred. Another approximately 40ml of water should be added. And the suspension stirred again thoroughly. More water may be added to the mixture as needed for desired consistency. The mixture should be taken within 1 hour. Apple juice and cranberry juice can be used instead of water to prepare the mixture. Other liquids with high potassium content should be avoided.
**Contraindications**: Hypersensitivity to active ingredient or to the excipient xanthan gum.
**Special warnings and precautions:** serum magnesium should be monitored for at least 1 month after initiating treatment, and magnesium supplementation considered in patients who develop low serum magnesium levels. A risk/benefit evaluation is required in patients with current or a history of severe gastrointestinal disorders, before and during treatment. When discontinuing Veltassa, serum potassium levels may rise, especially if RAAS inhibitor treatment is continued, so patients should be instructed not to discontinue therapy without consulting their physicians. Increases in serum potassium may occur as early as 2 days after the last dose. Serum potassium should be monitored when clinically indicated, including after changes are made to medicinal products that affect the serum potassium concentration (e.g. RAAS inhibitors or diuretics) and after the dose titration. Veltassa contains sorbitol as part of the counterion complex (4 g per 8.4 g of patiromer), therefore patients with hereditary problems of fructose intolerance should not take this medicine. Veltassa contains calcium as part of the counterion complex; calcium is partially released, some of which may be absorbed therefore a risk/benefit evaluation is required in patients at risk of hypercalcaemia. There are limited clinical data in patients with end-stage renal disease and in patients with serum potassium concentrations greater than 6.5 mmol/L.
**Overdose:** Veltassa is excreted after approximately 24-48 hours, based on average gastrointestinal transit time. Excessive doses may result in hypokalaemia, therefore serum potassium levels should be monitored.
**Special populations:** The use of Veltassa has not been studied in children under 18 years. Since there are no data from the use of patiromer in pregnant women, it is preferable to avoid the use of Veltassa during pregnancy. No special dose and administration guidelines are recommended for elderly population.
**Undesirable effects:** Common (≥1/100 to <1/10): Hypomagnesaemia, constipation, diarrhoea, abdominal pain, flatulence. Please consult the SmPC in relation to other undesirable effects.
**Legal category:** POM
**Price:** pack of 30 x 8.4g sachets = £172.50; pack of 30 x 16.8g sachets = £172.50
**MA Number:** EU/1/17/1179/001, EU/1/17/1179/004
**Date of Authorisation:** 19/07/2017
**MA Holder:** Vifor Fresenius Medical Care Renal Pharma France, 100-101 Terrasse Boieldieu, Tour Franklin La Défense 8, 92042 Paris La Défense Cedex, France



Document number: UK-PAT-1900126
Date of preparation: December 2019

**This medicine is subject to additional monitoring. Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Vifor Fresenius Medical Care Renal Pharma, care of Vifor Pharma Ltd. Tel: +44 1276 853633. E-mail: medicalinfo_UK@viforpharma.com**