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# POTASSIUM BINDING AGENTS IN THE INTENSIVE CARE UNIT: A NARRATIVE REVIEW

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## ABSTRACT

Hyperkalemia is a frequently encountered and potentially life-threatening electrolyte disturbance in critically ill patients, with reported prevalence rates of 20–40% in the intensive care unit (ICU) setting. While emergent stabilization with intravenous calcium gluconate, insulin-dextrose, and bicarbonate remains the cornerstone of acute management achieving sustained reduction in serum potassium requires the adjunctive use of potassium binding agents (PBAs). Historically, sodium polystyrene sulfonate (SPS) was the only available option; however, its significant adverse effect profile—including the risk of intestinal necrosis—has prompted a paradigm shift toward newer agents: patiromer and sodium zirconium cyclosilicate (SZC). This communication critically appraises pharmacology, evidence base, dosing strategies, monitoring requirements and practical considerations for using PBAs in the ICU. We highlight that SZC offers the most favorable profile for acute critical care, with rapid onset and renal-safe pharmacodynamics while patiromer remains suitable for sub-acute or chronic management. Appropriate patient selection, dose titration, drug–drug interaction screening and vigilant monitoring of electrolytes are essential to the safe use of these agents in the ICU.

**KEYWORDS:** hyperkalemia, potassium binding agents, sodium zirconium cyclosilicate, patiromer, sodium polystyrene sulfonate, intensive care unit, critical illness, renal replacement therapy.

## INTRODUCTION

Hyperkalemia is defined as a serum potassium concentration exceeding 5.5 mmol/L is among the most common and clinically significant electrolyte disturbances encountered in the intensive care unit.[12] Its prevalence in critically ill populations ranges from 20%-40% driven by an interplay of acute kidney injury (AKI), metabolic acidosis, massive cellular lysis, medication effects and impaired renal tubular function.[34] Even modest elevations in serum potassium

can precipitate life-threatening cardiac arrhythmias including ventricular fibrillation and asystole by disrupting the transmembrane electrochemical gradient essential for myocardial action potentials.[4]

Pathophysiology of hyperkalemia in critically ill patients is multifactorial. Renal insufficiency is documented in up to 57% of ICU admissions and is the single most important predisposing factor, as the kidney is responsible for excreting approximately 90% of daily potassium load.[56] Concurrent medications such as renin-angiotensin-aldosterone system (RAAS) inhibitors, beta-blockers, heparin, trimethoprim and calcineurin inhibitors further impair renal potassium handling.[28] Cellular release of intracellular potassium from tissue breakdown in rhabdomyolysis, tumor lysis syndrome, hemolysis, or massive blood transfusions adds substantially to the extracellular burden.[6]

The management of acute severe hyperkalemia ($K^+ > 6.5$ mmol/L or with ECG changes) involves a stepwise approach: membrane stabilization with intravenous calcium, redistribution with insulin-dextrose, inhaled beta-agonists and accelerated elimination via diuretics, renal replacement therapy or potassium binding agents (PBAs).[7] While the first two strategies act rapidly but transiently PBAs represent the only pharmacological option capable of reducing total body potassium load. The field has evolved considerably from the era dominated by sodium polystyrene sulfonate (SPS), with two newer agents patiromer and sodium zirconium cyclosilicate (SZC) which offer an improved efficacy, selectivity and safety profiles.[11,14]

This review aims to provide intensivists with a comprehensive, evidence-based guide to the appropriate selection, dosing, monitoring and pitfalls of PBA use in critically ill patients.

## Pharmacology of Potassium Binding Agents

### *Sodium Polystyrene Sulfonate (SPS)*

SPS (Kayexalate), a cation-exchange resin derived from polystyrene, has been used for hyperkalemia since the 1950s.

It exchanges sodium ions for potassium in the large intestine, theoretically binding 0.5–1 mEq of potassium per gram of resin.[15,16] However, the actual in vivo potassium-binding capacity of SPS is considerably lower than predicted and its clinical efficacy has been questioned by systematic reviews and a landmark placebo-controlled trial that found no significant benefit versus placebo at 24 hours.[15,16]

A major concern with SPS is its association with intestinal necrosis particularly in post-operative patients and when administered with sorbitol—historically used to prevent constipation.[17,18] A systematic review by Harel et al. documented significant gastrointestinal adverse events including colonic necrosis (often fatal), ischemic colitis, and obstruction.[18] Given these risks and the availability of superior alternatives, several guidelines now recommend restricting SPS use and avoiding it in postoperative patients, those with ileus or those with bowel hypoperfusion.[16]

### *Patiromer*

Patiromer is a spherical, non-absorbed polymer that works as a calcium-sorbitol cation exchanger. It selectively binds free potassium in the colon and distal gastrointestinal tract, releasing calcium in exchange.[13,14] Its selectivity for potassium over other cations (particularly sodium) avoids the sodium loading seen with SPS. The drug is delivered as an oral powder suspension.

The pivotal OPAL-HK trial demonstrated that patiromer significantly reduced serum potassium at 4 weeks (mean reduction −1.01 mmol/L, p<0.001) in patients with CKD on RAAS inhibitors.[14] A subsequent study by Pitt et al. confirmed its role in enabling continuation of RAAS therapy in heart failure patients.[13] The onset of action is approximately 7 hours, and hypomagnesemia is reported in approximately 9% of patients.[22] Importantly patiromer binds several oral medications (quinolones, levothyroxine, atenolol, metformin) necessitating a minimum 3-hour separation from other drugs.[14] It cannot be heated, limiting its use in enterally-fed ICU patients requiring warm formula.

***Sodium Zirconium Cyclosilicate (SZC / ZS-9)***

SZC is a non-polymer, inorganic crystalline compound with a microporous structure that acts as a highly selective potassium ion trap. Unlike exchange resins, SZC preferentially traps potassium and ammonium ions in the lumen with minimal exchange of sodium, calcium, or magnesium.[11,12] This high selectivity significantly reduces the risk of hypomagnesemia and hypocalcemia compared to SPS.

The HARMONIZE and AMETHYST-DN trials demonstrated that SZC achieves rapid and sustained potassium reduction, with a median time to normokalaemia of 2.2 hours at the 10 g dose.[12,20] This rapid onset is uniquely advantageous in the ICU setting. The drug is administered as an oral suspension three times daily for the first 48 hours (correction phase: 10 g TID), then once daily thereafter (maintenance phase: 5–10 g daily).[11] Importantly, SZC does not bind other medications significantly, simplifying polypharmacy management in the ICU.[20] The primary concern is sodium loading (approximately 400 mg Na per 10 g dose) which is clinically relevant in patients with fluid-overloaded heart failure or severe hyponatremia.[12]

***Calcium Polystyrene Sulphonate***

Calcium polystyrene sulphonate (CPS) is a cation-exchange resin that binds potassium in the gastrointestinal tract primarily in the colon releasing calcium ions in exchange and thereby promoting fecal potassium excretion.[26] Unlike sodium polystyrene sulphonate (SPS) CPS does not impose a sodium load, making it theoretically preferable in patients with heart failure, hypertension or fluid-overloaded states where sodium retention is undesirable.[27] Administered orally (15–30 g two to four times daily)/ rectally its onset of action is approximately 2–6 hours and clinical use spans chronic kidney disease, dialysis-dependent patients, and selected ICU settings. However, the evidence base remains limited to small trials and case series with concerns regarding intestinal necrosis which is less frequent than with SPS and a variable potassium-binding capacity reinforcing the preference for newer selective agents such as sodium zirconium cyclosilicate or patiromer whenever available.[28]

**Evidence Base in Critical Care**

The evidence base for PBAs in the ICU has improved significantly over the past decade, though most pivotal trials have been conducted in outpatient CKD or heart failure populations. Extrapolation to critically ill patients requires careful consideration of the distinctive ICU physiology.

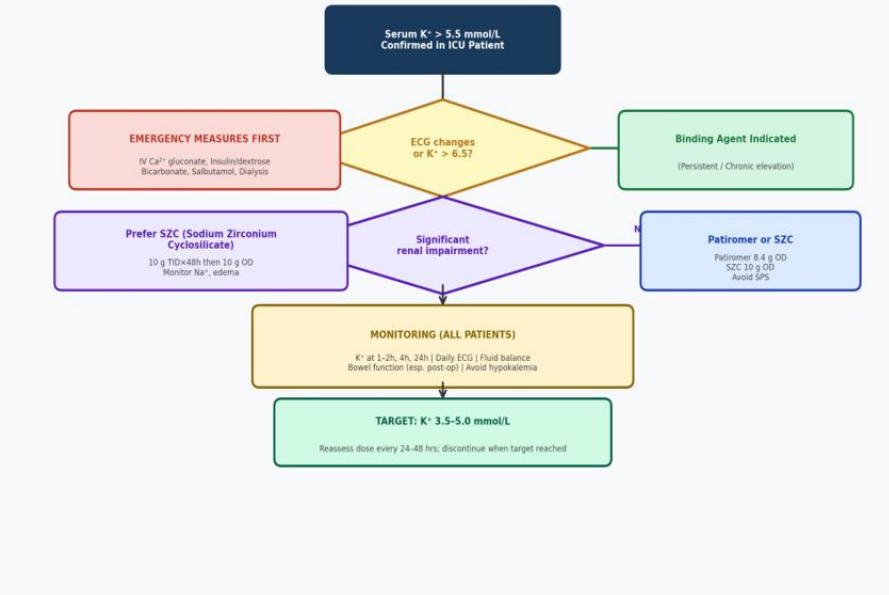
The ENERGIZE trial by Rafique et al. is among the few studies specifically designed for an acute emergency setting.[19,23] This randomized controlled trial compared SZC 10 g versus placebo in hyperkalemic emergency department patients simultaneously receiving standard-of-care (insulin-dextrose).SZC demonstrated significantly greater potassium reduction at 4 hours (−0.41 mmol/L vs −0.17 mmol/L; p=0.011) with more patients achieving

normokalaemia by 4 hours.[19] These findings support the incorporation of SZC as an adjunct to emergency hyperkalemia management.

For patiromer, the AMBER trial (Agarwal et al.) showed that it successfully enabled RAAS inhibitor continuation in patients with resistant hypertension and CKD—a frequent dilemma in the ICU as well.[21] The OPAL-HK study demonstrated durable potassium control over 52 weeks, suggesting a role in long-stay ICU patients or those transitioning to step-down/nephrology units.[14]

Regarding SPS the randomized trial by Lepage et al. found no statistically significant difference between SPS and placebo in potassium reduction at 24 hours, raising fundamental questions about the historical use of this agent[15] and coupled with documented gastrointestinal safety concerns, the evidence base no longer supports SPS as a first-line or routine agent in the ICU.[16-18]

In patients requiring renal replacement therapy (RRT) PBAs may reduce the interdialytic potassium accumulation and lower the frequency of urgent dialysis sessions. However, randomized data in these specific subsets is currently limited.[24,25]




*ICU decision algorithm for potassium binding agent selection and monitoring.*

**Dosing and Monitoring in the ICU**

**Dosing Protocols**

In the ICU dosing must balance the urgency of potassium reduction against the risk of over-correction and side effects. For SZC the correction dose of 10 g three times daily for 48 hours is well-validated by trial data and should be the preferred approach in acute hyperkalemia ($K^+$ 5.5–6.5 mmol/L without life-threatening ECG changes).[11,12] Following the correction phase, the maintenance dose of 5–10 g once daily may be titrated based on repeat serum potassium values every 12–24 hours. The drug is suspended in 45 mL of water and is compatible with nasogastric tube administration in intubated patients.

Patiromer dosing begins at 8.4 g once daily, titrated in 8.4 g increments every 7 days to a maximum of 25.2 g/day[14,22] and given its prolonged onset (approximately 7 hours) patiromer is best suited for sub-acute hyperkalemia in the ICU

($K^+$ 5.5–6.0 mmol/L, stable hemodynamics)/for maintenance therapy in patients with recurrent hyperkalemia. It should not replace emergent measures. Use in patients with ileus or limited gut motility should be avoided as absorption of the vehicle may be unpredictable.

SPS, if used at all, should be reserved for situations where SZC and patiromer are unavailable. The oral dose is 15–60 g in 20% sorbitol, though sorbitol should be avoided in postoperative patients.[16,17] Rectal administration (30–60 g in water enema) may be considered in patients unable to tolerate oral/enteral medications.

**Monitoring Parameters**

Periodic monitoring is mandatory in the ICU. Serum potassium should be rechecked at 1–2 hours after SZC administration (to detect rapid correction) at 4 hours and at 24 hours.[11] For patiromer, repeat levels at 4 and 24 hours are appropriate given its delayed onset. ECG monitoring should be continuous in all patients with $K^+ > 6.0$ mmol/L or ECG abnormalities and repeated at each potassium check thereafter. Serum magnesium should be monitored daily in patients receiving patiromer; serum sodium should be tracked in fluid-restricted patients receiving SZC.[12,14] Bowel function must be documented daily as constipation predisposes to drug accumulation and rectal impaction.

The target serum potassium in the ICU is 3.5–5.0 mmol/L. Hypokalemia should be actively avoided as it equally predisposes to cardiac arrhythmias. Dose reduction or discontinuation is warranted when $K^+$ falls below 4.0 mmol/L on two successive measurements. Patients on digoxin require especially vigilant monitoring, as hypokalemia dramatically enhances digoxin toxicity.[6,7]

**Special Considerations in the ICU**

**Acute Kidney Injury**

AKI is the most common setting of hyperkalemia in the ICU. In oliguric AKI (urine output < 0.5 mL/kg/hr) gastrointestinal excretion becomes the primary route of potassium elimination, making PBAs especially relevant.[25]

SZC is preferred because of its rapid onset and independence from renal function for efficacy. In patients with AKI requiring intermittent hemodialysis, SZC given between sessions can significantly reduce interdialytic potassium rise.[20]

However, PBAs are not a substitute for RRT when urgent dialysis is indicated.

**Post-Cardiac Surgery Patients**

Hyperkalemia is common after cardiac surgery, driven by cardioplegia, blood transfusions, and perioperative AKI.[5] In this context, intestinal ischemia, a recognized complication is an absolute contraindication for SPS.[18] SZC is the agent of choice. Care should be taken regarding sodium loading with SZC in patients with reduced cardiac output, and close hemodynamic monitoring is necessary.

**Sepsis-Associated Hyperkalemia**

Sepsis causes hyperkalemia through several mechanisms: AKI, metabolic acidosis, rhabdomyolysis, and impaired insulin signaling.[25] In this population, ongoing fluid resuscitation may paradoxically mask hyperkalemia transiently. Post hemodynamic stabilization, persistent hyperkalemia should be addressed with PBAs. The acidosis-driven

component will often respond to treatment of the underlying infection and metabolic normalization hence, PBA use should be reassessed at frequent intervals.

**Drug Interactions and Enteral Nutrition**

In ICU, patients frequently receive multiple medications enterally or via nasogastric tubes. Patiromer significantly binds to several drugs including fluoroquinolones, levothyroxine, cyclosporine, and metoprolol; all co-administered medications must be given at least 3 hours apart.[14] SZC has minimal documented drug interactions, offering a significant practical advantage.[20] Standard ICU enteral nutrition formulas are high in potassium (typically 40–60 mEq/day) and formula modification or switching to low-potassium formulas should be considered as a complimentary strategy.

**Algorithmic Approach for the Intensivist**

Based on available evidence, the following stepwise approach is recommended for PBA use in the ICU (Figure 2):

Step 1: **Confirm and classify hyperkalemia:** Repeat serum potassium to exclude pseudo hyperkalemia (hemolysis, prolonged tourniquet time). Classify severity: mild (5.5–5.9), moderate (6.0–6.4) or severe (≥6.5 mmol/L).[6]

Step 2: **Perform a 12-lead ECG:** Any ECG changes (peaked T waves, PR prolongation, QRS widening, sine-wave pattern) mandate immediate stabilization with intravenous calcium gluconate (10 mL of 10% solution over 2–3 minutes) before PBA initiation.[7]

Step 3: **Apply redistribution measures:** Insulin 10 units with 50 mL of 50% dextrose IV, sodium bicarbonate (in metabolic acidosis) and inhaled salbutamol (2.5–5 mg nebulized). These lower potassium within 15–30 minutes but do not reduce total body potassium.[7]

Step 4: **Initiate PBA for elimination:** Once life-threatening ECG changes are managed initiate SZC 10 g TID for 48 hours (Or patiromer 8.4 g OD if SZC unavailable and onset < urgency required). Avoid SPS in ICU patients.[11,14]

Step 5: **Consider RRT:** For refractory hyperkalemia ($K^+$ > 6.5 mmol/L not responding to medical management/ anuric AKI) continuous RRT (CRRT)/ emergency hemodialysis is the most effective and rapid intervention.[25]

Step 6: **Monitor and titrate:** Reassess serum $K^+$ at 1–2 h, 4 h and 24 h. Adjust PBA dose when target range (3.5–5.0 mmol/L) is reached. Discontinue PBA once normokalaemia is achieved and dietary/pharmacological precipitants have been addressed.

**Emerging Evidence and Future Directions**

Clinical trial programs continue to expand the evidence base for PBAs in critical populations. Head-to-head trials comparing SZC versus patiromer in the emergency and ICU settings such as the comparative effectiveness arm of ENERGIZE trial will help further refine selection criteria.[19] Long-term data on SZC in AKI-on-CKD patients across a full course of illness are awaited from ongoing registry studies.[20] There is emerging interest in the use of PBAs to facilitate continuation of lifesaving RAAS inhibitors in CKD patients who have previously had to discontinue these agents due to hyperkalemia as a strategy validated in outpatients which may translate to step-down ICU management.[21,24]

Biomarker-driven dosing using urinary potassium-creatinine ratios to predict PBA dose requirements is an area of exploratory research. Machine learning–assisted hyperkalemia risk models may eventually help identify ICU patients at highest risk allowing preemptive rather than reactive PBA use.

## CONCLUSION

Potassium binding agents represent an essential, yet often underappreciated component of the hyperkalemia management armamentarium in the ICU. The field has evolved markedly, and the historical default to SPS can no longer be justified given its limited evidence base and the well-documented risk of intestinal necrosis.[16,18] Sodium zirconium cyclosilicate with its rapid onset, high selectivity, minimal drug interactions and compatibility with nasogastric administration is the preferred agent for acute and sub-acute hyperkalemia in critically ill patients.[11,12,19]

Patiromer occupies a complimentary role in maintenance management and in patients transitioning from the ICU.[13,14]

A rational, algorithmic approach incorporating electrolyte monitoring, ECG surveillance, awareness of drug interactions, and timely escalation to renal replacement therapy will optimize patient outcomes.

As newer agents undergo further validation in critical care–specific populations the intensive care specialists must remain abreast of evolving evidence to provide safe, individualized and effective care for this complex and high-risk electrolyte disorder.

## REFERENCES

1. Weir MR, Rolfe M. Potassium homeostasis and renin-angiotensin-aldosterone system inhibitors. Clin J Am Soc Nephrol, 2010; 5(3): 531-48.
2. Palmer BF. Managing hyperkalemia caused by inhibitors of the renin-angiotensin-aldosterone system. N Engl J Med, 2004; 351(6): 585-92.
3. Kovesdy CP. Management of hyperkalaemia in chronic kidney disease. Nat Rev Nephrol, 2014; 10(11): 653-62.
4. Montague BT, Ouellette JR, Buller GK. Retrospective review of the frequency of ECG changes in hyperkalemia. Clin J Am Soc Nephrol, 2008; 3(2): 324-30.
5. Einhorn LM, Zhan M, Hsu VD et al. The frequency of hyperkalemia and its significance in chronic kidney disease. Arch Intern Med, 2009; 169(12): 1156-62.
6. Rastegar A, Soleimani M. Hypokalaemia and hyperkalaemia. Postgrad Med J., 2001; 77(914): 759-64.
7. Mahoney BA, Smith WA, Lo DS et al . Emergency interventions for hyperkalaemia. Cochrane Database Syst Rev., 2005; (2): CD003235.
8. Pitt B, Zannad F, Remme WJ et al. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. N Engl J Med, 1999; 341(10): 709-17.
9. Bakris GL, Weir MR, Secic M et al. Differential effects of calcium antagonist subclasses on markers of nephropathy progression. Kidney Int, 2004; 65(6): 1991-2002.
10. Laureati P, Xu Y, Trevisan M et al. Initiation of RAAS inhibitors and clinical outcomes in advanced CKD: a nationwide observational cohort study. Nephrol Dial Transplant, 2021; 36(10): 1849-61.
11. Packham DK, Rasmussen HS, Lavin PT et al. Sodium zirconium cyclosilicate in hyperkalemia. N Engl J Med, 2015; 372(3): 222-31.
12. Kosiborod M, Rasmussen HS, Lavin P et al. Effect of sodium zirconium cyclosilicate on potassium lowering for 28 days among outpatients with hyperkalemia: the HARMONIZE randomized clinical trial. JAMA, 2014; 312(21): 2223-33.

13. Pitt B, Bakris GL, Bushinsky DA et al. Effect of patiromer on reducing serum potassium and preventing recurrent hyperkalaemia in patients with heart failure and chronic kidney disease on RAAS inhibitors. Eur J Heart Fail, 2015; 17(10): 1057-65.
14. Weir MR, Bakris GL, Bushinsky DA et al. Patiromer in patients with kidney disease and hyperkalemia receiving RAAS inhibitors. N Engl J Med, 2015; 372(3): 211-21.
15. Lepage L, Dufour AC, Doiron J et al. Randomized clinical trial of sodium polystyrene sulfonate versus placebo in treatment of mild hyperkalemia in CKD. Clin J Am Soc Nephrol, 2015; 10(12): 2136-42.
16. Sterns RH, Grieff M, Bernstein PL. Treatment of hyperkalemia: something old, something new. Kidney Int, 2016; 89(3): 546-54.
17. Watson M, Abbott KC, Yuan CM. Damned if you do, damned if you don't: potassium binding resins in hyperkalemia. Clin J Am Soc Nephrol, 2010; 5(10): 1723-6.
18. Harel Z, Harel S, Shah PS et al. Gastrointestinal adverse events with sodium polystyrene sulfonate (Kayexalate) use: a systematic review. Am J Med, 2013; 126(3): 264.e9-24.
19. Rafique Z, Peacock WF, Armahizer M et al. Sodium zirconium cyclosilicate versus patiromer for treating hyperkalemia in the emergency setting: the ENERGIZE randomized trial. Acad Emerg Med, 2020; 27(6): 475-83.
20. Roger SD, Spinowitz BS, Lerma EV et al. Efficacy and safety of sodium zirconium cyclosilicate for treatment of hyperkalemia: an 18-month study. Am J Nephrol, 2019; 50(6): 473-80.
21. Agarwal R, Rossignol P, Garza D, Mayo MR, Warren S, Lee T, et al. Patiromer versus placebo to enable spironolactone use in patients with resistant hypertension and chronic kidney disease (AMBER): a phase 2, randomised, double-blind, placebo-controlled trial. Lancet, 2019; 394(10208): 1540-50.
22. Bushinsky DA, Williams GH, Pitt B et al. Patiromer induces rapid and sustained potassium lowering in patients with chronic kidney disease and hyperkalemia. Kidney Int, 2015; 88(6): 1427-33.
23. Peacock WF, Rafique Z, Vishnevskiy K et al. Emergency potassium normalization treatment including sodium zirconium cyclosilicate: a phase II, randomized, double-blind, placebo-controlled study (ENERGIZE). Acad Emerg Med, 2020; 27(6): 475-483.
24. Zannad F, Rossignol P, Stough WG et al. New approaches to hyperkalemia in patients with indications for renin angiotensin aldosterone inhibitor therapy. Prog Cardiovasc Dis, 2016; 58(4): 391-9.
25. Legrand M, Dupuis C, Simon C et al. Association between systemic hemodynamics and septic acute kidney injury in critically ill patients: a retrospective observational study. Crit Care, 2013; 17(6): R278.
26. Scherr L, Ogden DA, Mead AW et al. Management of hyperkalemia with a cation-exchange resin. N Engl J Med., 1961; 264(3): 115–9.
27. Batterink J, Cessford TA, Taylor RA. Pharmacological management of hyperkalemia. Can Fam Physician, 2015; 61(7): 595–602.
28. Chaitman M, Ng T, Neville H et al. Gastrointestinal complications associated with sodium and calcium polystyrene sulfonate use in hospitalized patients. Am J Ther, 2016; 23(6): e1581–5.