# NEW POTASSIUM BINDER

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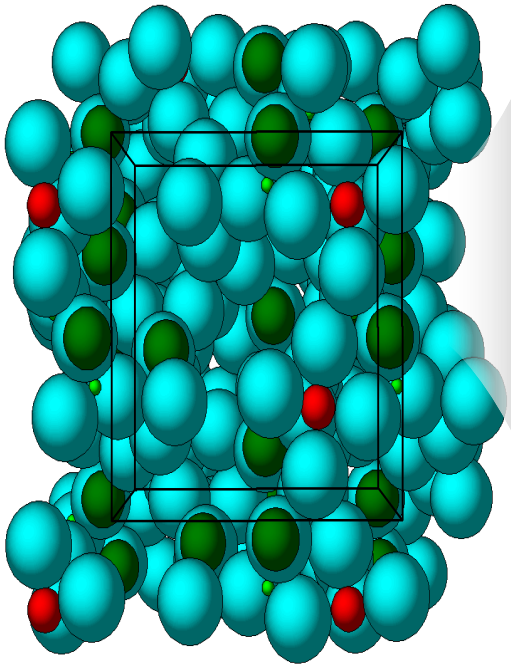
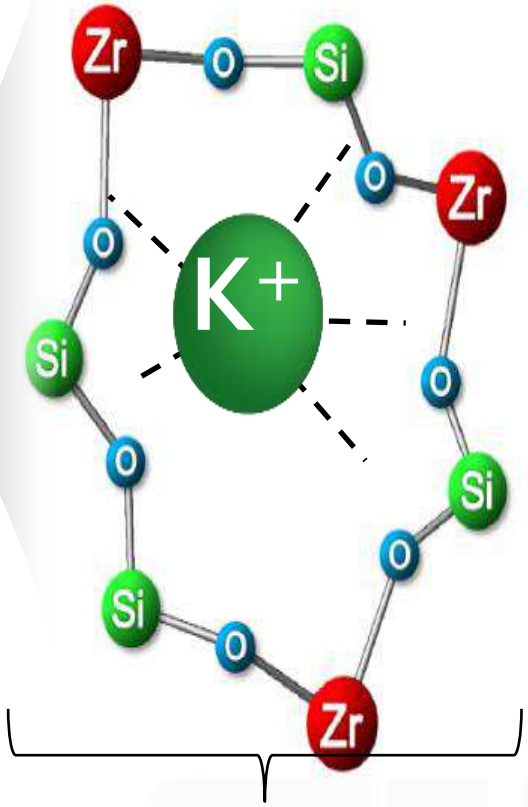
# SODIUM ZIRCONIUM CYCLOSILICATE [SZC]

## Crystal Structure






Average Binding-Site Width: 3 Å

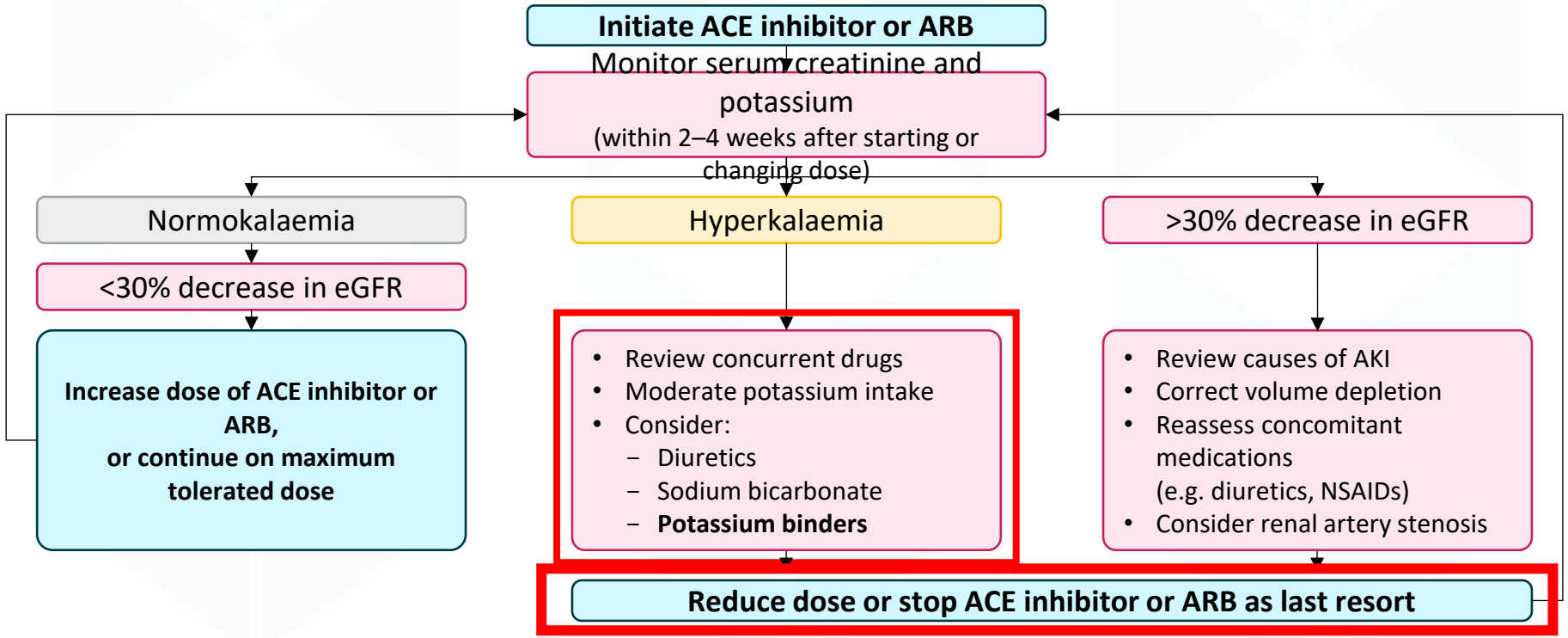
- Inorganic crystalline potassium binder; not a polymer
- Exchanges $H^+$ and $Na^+$ for $K^+$
- Highly selective for $K^+$; binding site width and $K^+$ ionic diameter are similar
- Insoluble, highly stable, and does not expand in water
- Not systemically absorbed

- O = oxygen atom; Si = silicon atom; SZC = sodium zirconium cyclosilicate; Zr = zirconium atom.
- Stavros F et al. *PLoS One*. 2014;9:e114686.

| | Traditional Potassium Binder | Novel Potassium Binder | Novel Potassium Binder |
|---|---|---|---|
| | Calcium polystyrene sulfonate (CPS) | Sodium zirconium cyclosilicate (SZC)▼ | Patiromer |
| **Mechanism** | Nonspecific calcium cation–exchange resin[4] | Selective potassium binding in exchange for sodium and hydrogen[6] | Potassium binding in exchange for calcium |
| **Onset** | Action may be delayed for 1 to 2 days[4] | 1 hour[8] | 7 hours |
| **Dosing** | 15 g orally 3 to 4 times daily[5]<br><br>30 g given as retention enema once daily[5] | 10 g orally 3 times daily for a maximum of 72 hours (starting dose)[8.b]<br>5 g orally once daily (recommended starting maintenance dose)[8] | 8.4gm QD, titrate upto 16.8gm or 25.2gm |
| **Indication** | Treatment of HK associated with anuria or severe oliguria and treatment of HK in patients requiring dialysis[5] | Treatment of HK in adults; there is limited experience in patients with serum $K^+$ levels greater than 6.5 mmol/L[8] | Treatment of HK in adults and paediatrics |
| **Location** | Colon[4] | Entire intestinal tract[6] | Colon |
| **Adverse events** | Cases of intestinal necrosis, which may be fatal, and other serious GI adverse events have been reported[5] | Hypokalaemia and oedema-related events[8] | Hypomagnesemia, GI adverse effects |
| **Drug Interactions** | Antacids, laxatives, digitalis, sorbitol, lithium, levothyroxine[5]<br>Administer at least 3 hours before or 3 hours after other oral medications[5] | Administer at least 2 hours before or 2 hours after oral medications with clinically meaningful gastric pH-dependent bioavailability[8] | None |

- [a] SPS was FDA approved prior to the Kefauver-Harris Drug Amendments in 1962, which required drug manufacturers to prove effectiveness of their product.[9]
- ▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 of the SmPC for how to report adverse reactions.[8] [b]Dose differs for patients on haemodialysis- refer to SmPC for more information.[8] References and abbreviations in slide notes.

# Hyperkalaemia associated with use of RAAS inhibitors can often be managed by measures to reduce the serum potassium levels rather than decreasing the dose or stopping RAAS inhibitors

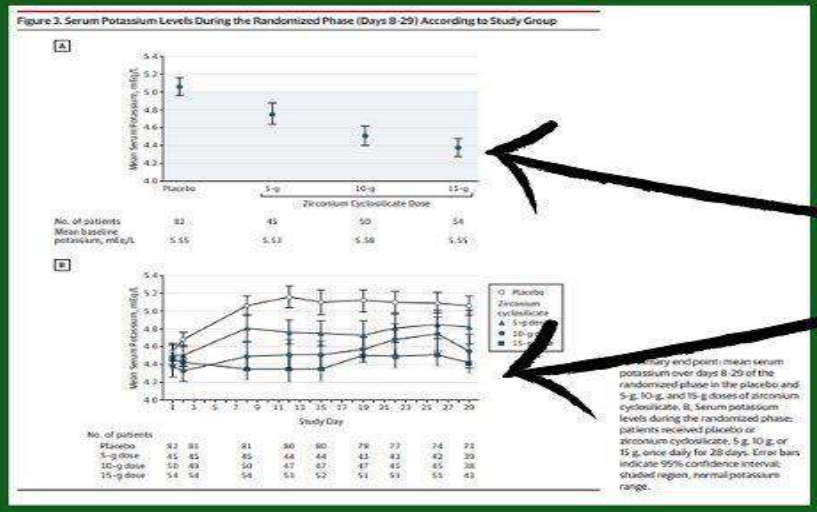



**Note: ACE inhibitor or ARB should only be reduced or stopped after measures outlined above have failed**

ACE, angiotensin-converting enzyme; AKI, acute kidney injury; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; KDIGO, Kidney Disease: Improving Global Outcomes; NSAID, non-steroidal anti-inflammatory drug; RAAS, renin–angiotensin–aldosterone system; T2D, Type 2 diabetes

Kidney Disease: Improving Global Outcomes. 2024 Guidelines

# HARMONIZE Trial

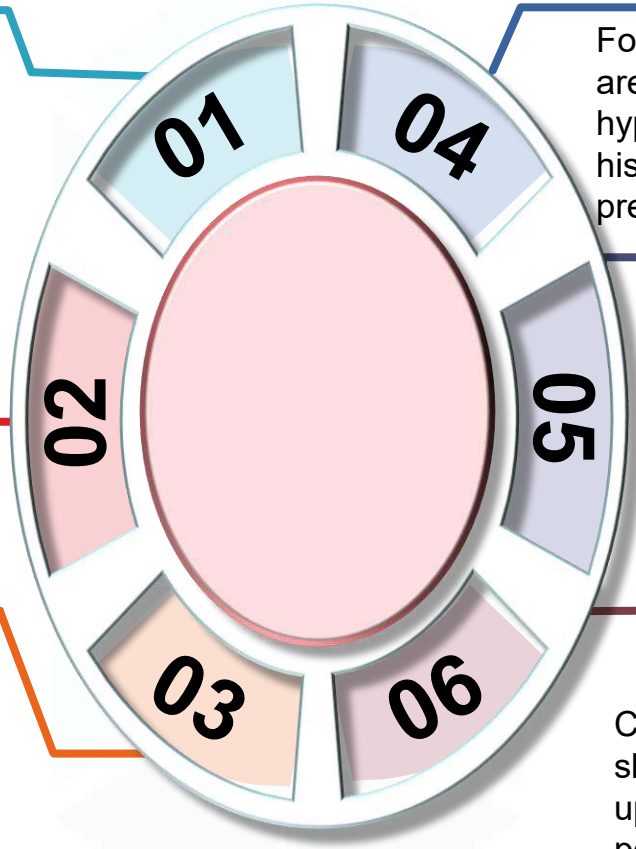



Treatment Arm

- N=237 patients
- Patients with persistent hyperkalemia entered a 48-hour open-label run-in during which they received Sodium Zirconium Cyclosilicate 10g 3 times daily
- K >5.1
- 69% had CKD
- 70% per taking RAASi
- documented hyperkalemia that led to D/C of RAASi or beta-blocker within 6 months.

**Results: Sodium Zirconium Cyclosilicate is safe and efficacious in the treatment of asymptomatic hyperkalemia. A dose-dependent relationship was observed, with higher doses achieving greater normalization of hyperkalemia, but with a greater propensity for side effects including hypokalemia.**

# The recent Delphi consensus resulted in the following recommendations regarding hyperkalaemia




01 Hyperkalaemia should be recognised as a predictable, treatable and manageable side effect of optimal HF / CKD therapy in people with a history or at high risk for hyperkalaemia

02 RAASi use should not be de-escalated or discontinued due to hyperkalaemia unless alternative measures of hyperkalaemia management have been optimised

03 Novel potassium binders should be the preferred agent to manage hyperkalaemia and should be used to enable and maintain optimised RAASi therapy

04 For high-risk individuals that are currently not hyperkalaemic, a thorough history is critical to inform preventative measures

05 Closer cross-specialty collaboration would help optimise outcomes for individuals with cardiorenal disease. Clinical teams should be encouraged and supported to identify suitable methods to achieve this within their care setting

06 Consistent treatment approach should be the goal of new and updated guidelines that support people with cardiorenal disease, and cross-specialty support should be sought for these to ensure aligned clinical practice

CKD, chronic kidney disease; HF, heart failure; RAASi, renin–angiotensin–aldosterone system inhibitor

Burton JO, et al. *Eur J Heart Fail* 2022;24:1467–1477