Therapeutic Advances in Hyperkalemia

A Pharmacist's Guide to Patient Identification and Treatment

Faculty

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Disclosures

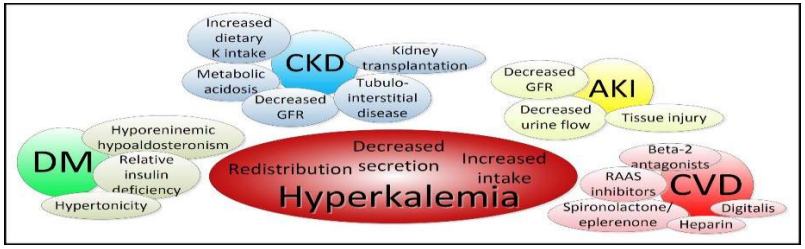
Dr. Grabe has disclosed no relevant financial relationships with any commercial interest.

Dr. Grabe will be discussing the following off-label: Patiromer and sodium zirconium cyclosilicate (formerly ZS-9) – hyperkalemia

Learning Objectives

- Outline the clinical and socioeconomic consequences of unrecognized and undertreated chronic hyperkalemia
- Identify the risk factors and pathophysiologic mechanisms associated with the development of hyperkalemia in key patient populations
- Evaluate the latest clinical data surrounding new and emerging potassium binding agents with respect to mechanisms of action, efficacy, safety, indications, and therapeutic placement in hyperkalemia management strategies
- Advance the long-term management of hyperkalemia in pharmacy practice through measures that facilitate at-risk patient monitoring, promote patient/provider education, and integrate newer therapies for optimal patient outcomes

Hyperkalemia



DM = diabetes mellitus; CKD = chronic kidney disease; GFR = glomerular filtration rate; AKI = acute kidney injury; CVD = cardiovascular disease.
Kovesdy CP. *Am J Med*. 2015;128(12):1281-1287.

Epidemiology and Cost of Hyperkalemia

- General population
  - 76,028 ED visits (2014)
  - 46% admitted
  - Average LOS, 3.3 days
  - Cost $29,667 per stay
- CKD
  - Depends on severity
  - Depends on definition

Time Spent at Serum Potassium Levels

eGFR (mL/min/1.73 m²)	Serum K⁺ Level mEq/L		
	5.0-5.4	**5.5-5.9**	**≥6.0**
50-59	11.3	1.7	0.2
40-49	14.6	2.7	0.3
30-39	18.9	4.5	0.7
<30	23.0	7.6	1.8

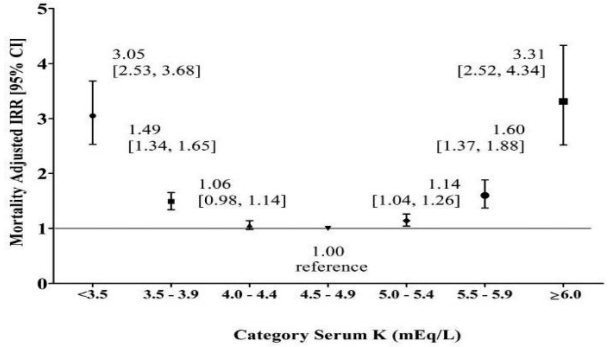
ED = emergency department; LOS = length of stay; eGFR = estimated glomerular filtration rate.
AHRQ Agency for Healthcare Research and Quality [website]. http://hcupnet.ahrq.gov/. Accessed May 14, 2018. Luo J, et al. *Clin J Am Soc Nephrol*. 2016;11(1):90-100.

Preventable Hospitalizations

- Measurement of inpatient encounters for **ambulatory care sensitive conditions**
  - Hyperkalemia, HF, malignant hypertension, volume overload
- Patients included if they had CKD (eGFR, 15-60 mL/min/1.73 m²)
- 1 in 4 CKD hospitalizations linked to ambulatory care sensitive conditions
- Majority of encounters were related to HF or hyperkalemia

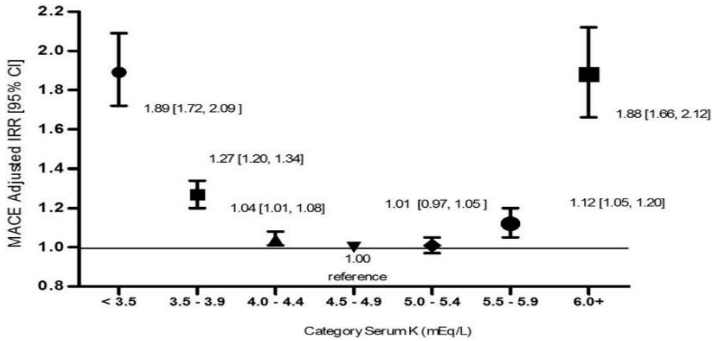
HF = heart failure.
Ronksley PE, et al. *Clin J Am Soc Nephrol*. 2016;11(11):2022-2031.

Associations between Serum K+ and Mortality



Luo J, et al. *Clin J Am Soc Nephrol*. 2016;11:90-100.

Major Adverse CV Events (MACE) According to Serum K+



Luo J, et al. *Clin J Am Soc Nephrol*. 2016;11:90-100.

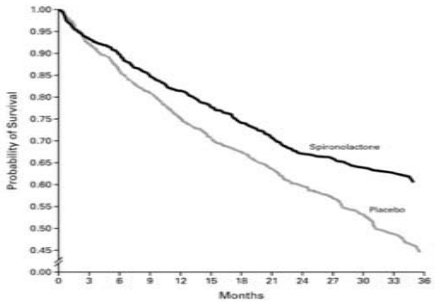
Drugs of Choice for Conditions

- Hypertension
  - ACEI
  - ARB
- HF
  - ACEI
  - ARB
  - Aldosterone antagonists
- Diabetic nephropathy
  - ACEI
  - ARB
- Strategies for managing hypertension
  - Maximize dose of one agent, then add a second agent
  - Start one agent, then add a second agent before maximal dose
  - Start two agents and titrate dose
  - Follow the Dietary Approach to Stop Hypertension (DASH) diet

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; DASH = dietary approach to stop hypertension.

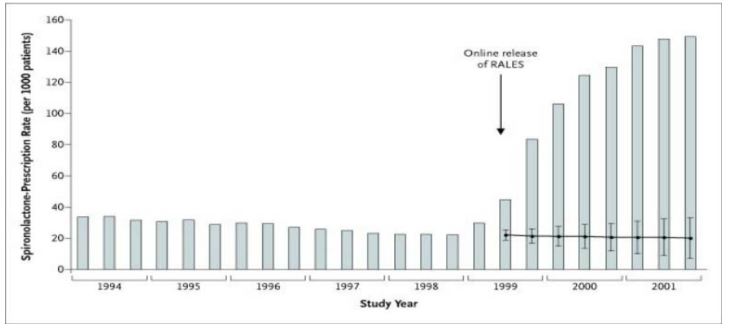
RALES

- Severe HF
- Study terminated early
- 31% reduction in death



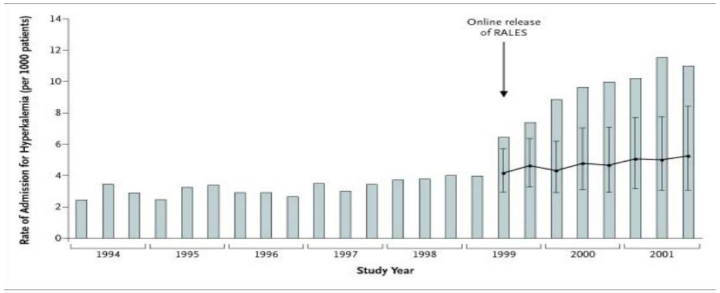
RALES = Randomized Aldactone Evaluation Study.
Pitt B, et al. *N Engl J Med*. 1999;341(10):709-717.

Use of Spironolactone Increased Dramatically



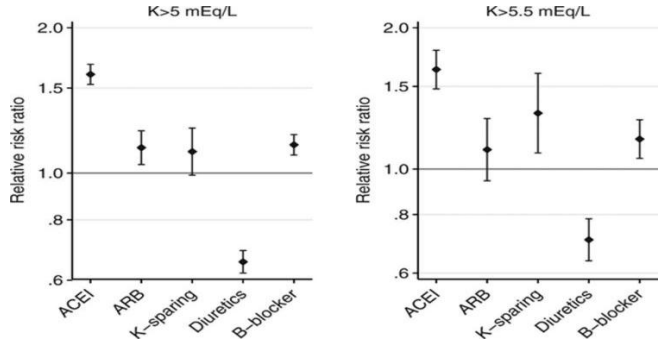
Juurlink DN, et al. *N Engl J Med*. 2004;351:543-551.

So Did Hyperkalemia



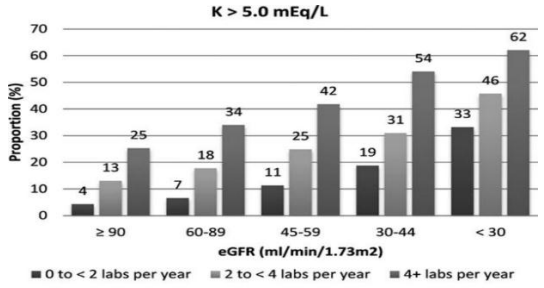
Juurlink DN, et al. *N Engl J Med*. 2004;351:543-551.

Risk of Hyperkalemia Associated with Antihypertensive Medication Classes



K = potassium.
Chang AR, et al. *Hypertension*. 2016;67:1181-1188.

Proportion Experiencing Hyperkalemia over 3 Years by eGFR and Frequency of Potassium Testing



Chang AR, et al. *Hypertension*. 2016;67:1181-1188.

Case Study

- 53-year-old man with CKD stage 3b (eGFR, 34 mL/min/1.73 m^2), type 2 diabetes mellitus, hypertension, dyslipidemia, and proteinuria
  - Current medications
    - Lisinopril 40 mg daily
    - Hydrochlorothiazide 25 mg daily
    - Atorvastatin 10 mg daily
    - Aspirin EC 81 mg daily
    - Metformin 1000 mg twice daily
    - Linagliptin 5 mg daily
  - Recent laboratory results show hyperkalemia with a serum potassium level of 5.5 mEq/L

Based on the clinical scenario, which of the following actions should be taken?

A. Reduce dose of lisinopril
B. Discontinue lisinopril
C. Increase dose of hydrochlorothiazide
D. Add furosemide 40 mg daily
E. Add sodium polystyrene sulphonate

Actions Taken after Hyperkalemia

Action	K >5.0 mEq/L	K >5.5 mEq/L	Control
ED visit	1.2%	3.1%	0.7%
Repeat serum K measurement	18.4%	44.3%	0.0%
Rx SPS	0.7%	4.7%	0.0%
Rx/Incr diuretic	5.6%	9.2%	2.5%
D/C ACEI or ARB	10.5%	24.3%	4.8%
Decr ACEI or ARB	2.6%	4.8%	1.2%
D/C K-sparing diuretic	23.0%	48.5%	7.5%
Decr K-sparing diuretic	1.4%	1.1%	0.5%

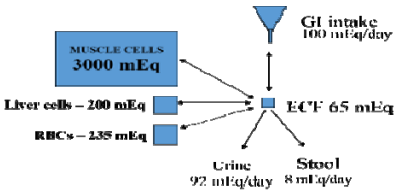
SPS = sodium polystyrene sulphonate; D/C = discontinuation.
Chang AR, et al. *Hypertension*. 2016;67:1181-1188.

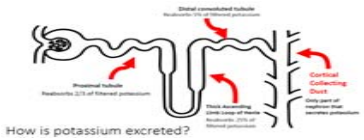
Which part of the nephron is responsible for potassium secretion?

A. Proximal convoluted tubule
B. Loop of Henle
C. Distal convoluted tubule
D. Cortical collecting duct

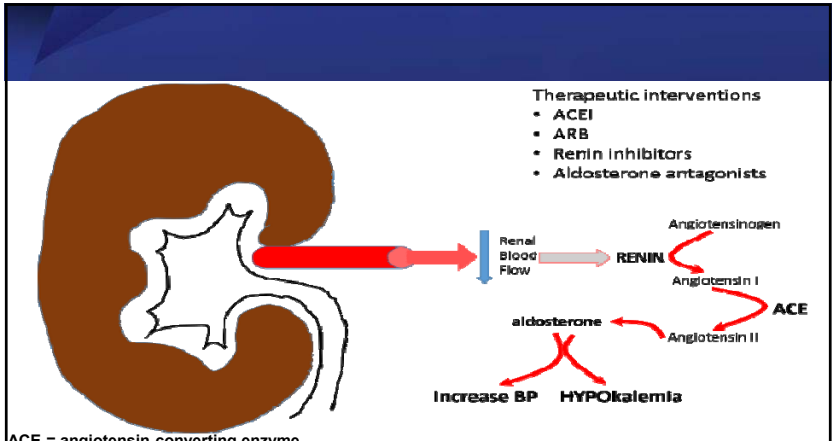
Potassium Handling: What Is Normal?

- Intracellular cation (120-153 mEq/L)
  - Extracellular (3.5-4.5 mEq/L)
- Typical 70-kg man has 4000 mEq
  - 56 mEq = extracellular
  - Think about typical doses for potassium supplement
- Average US diet = 40 mEq/d
- Recommended daily allowance = 90 mEq/d

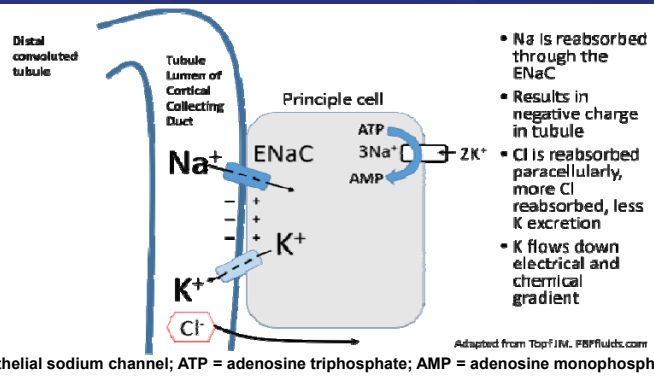




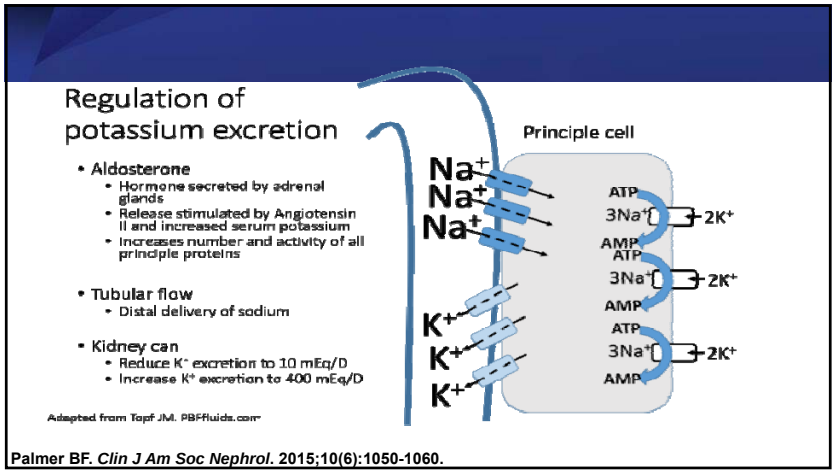
RBC = red blood cell; GI = gastrointestinal; ECF = extracellular fluid.
Palmer BF, et al. *Adv Physiol Educ*. 2016;40:480-490.



ACE = angiotensin-converting enzyme.
Subramanya A, et al. *Clin J Am Soc Nephrol*. 2014;9(12):PMC4255408.



ENaC = epithelial sodium channel; ATP = adenosine triphosphate; AMP = adenosine monophosphate.
Subramanya A, et al. *Clin J Am Soc Nephrol*. 2014;9(12):PMC4255408.



Palmer BF. *Clin J Am Soc Nephrol*. 2015;10(6):1050-1060.

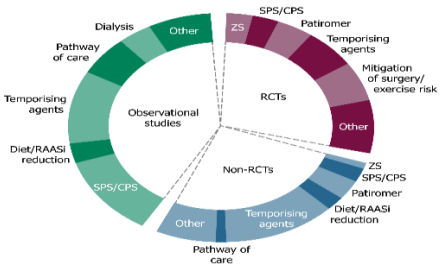
Hyperkalemia Waits for No One

- Severe muscle weakness
- Electrocardiogram changes
- Conduction abnormalities
- Arrhythmia
- Reduced urinary acid secretion

UpToDate [website]. Mount DB. Clinical manifestations of hyperkalemia in adults. https://www.uptodate.com/contents/clinical-manifestations-of-hyperkalemia-in-adults. Last updated December 12, 2017. Accessed May 14, 2018.

Management of Hyperkalemia

Management of Hyperkalemia



ZS = sodium zirconium cyclosilicate; SPS/CPS = sodium/calcium polystyrene sulphonate; RCT = randomized controlled trial; RAASi = renin-angiotensin-aldosterone system inhibitor.
Palaka E, et al. *Int J Clin Pract*. 2018;72(2):e13052.

Which of the following serious adverse events related to SPS resulted in an FDA safety labeling change?

A. Exacerbation of HF
B. Elevation of BP
C. Development of colonic necrosis
D. Risk of AKI

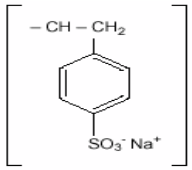
FDA = US Food and Drug Administration; BP = blood pressure.

Current Therapies

- Current therapies for acute and chronic management of hyperkalemia
  - Temporizing agents
    - Insulin/Dextrose
    - Beta agonists (eg, albuterol)
    - Hemodialysis
  - Sodium polystyrene sulfonate (SPS)
  - Organic polymer resin patiromer calcium sorbitex (patiromer)
  - Sodium zirconium cyclosilicate (formerly ZS-9)

Sodium Polystyrene Sulfonate (SPS)

- Benzene, diethenyl-polymer, with ethenylbenzene, sulfonated, sodium salt
- Contraindications: Hypokalemia, hypersensitivity to polystyrene sulfonate resins, obstructive bowel disease, neonates with reduced gut motility, oral administration in neonates
- Administration: Oral and rectal (enema)
- Available as powder, suspension, enema
- Store at 25° C (77° F)
- Average daily adult dose of resin: 15 g to 60 g
- Administer 15 g 1 to 4 times daily
- Cost: 454 gram jar is $50-$150



US Food and Drug Administration [website]. Drugs@FDA: FDA approved drug products. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&applno=011287. Accessed May 14, 2018. Elliott W, et al. Relias [website]. Pharmacology update. Patiromer for oral suspension (veltassa). https://www.ahcmedia.com/articles/137411-patiromer-for-oral-suspension-veltassa . Accessed May 14, 2018.

SPS: The Issues List

- No rigorous clinical trials to determine efficacy and safety
- Takes several hours for reduction in serum potassium
- Questionable utility in emergent hyperkalemia
- Questionable efficacy when not combined with sorbitol
- Questionable safety concerns
- Drug interactions
- Mixing, dosing, and palatability

Batterink J, et al. *Can J Hosp Pharm*. 2015;68(4):296-303.

SPS Clinical Trial Data

- Approval based on study of 32 patients
  - Hyperkalemia, azotemia, hemodialysis not yet available
  - Serum potassium decreased by 0.9 mEq/L in 24 hours
- Retrospective analysis of 157 patients
  - Mean serum potassium, 5.9 mEq/L
  - Reduction of 0.7-1.1 mEq/L
- Most often combined with sorbitol
- ClinicalTrials.gov identifier NCT01866709: Safety and efficacy of SPS in hyperkalemia
  - Prematurely terminated for safety reasons due to high frequency of adverse events in SPS group

Flinn RB, et al. *N Engl J Med.* 1961;264:111-115. Batterink J, et al. *Can J Hosp Pharm.* 2015;68(4):296-303. Scherr L, et al. *N Engl J Med.* 1961;264:115-119. ClinicalTrials.gov [website]. https://clinicaltrials.gov/ct2/show/NCT01866709?term=sodium+polystyrene+sulfonate&rank=2. Accessed May 14, 2018.

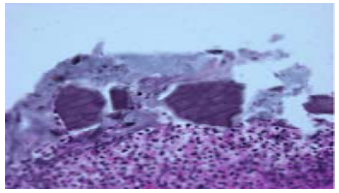
SPS Clinical Trial Data

- Prospective, randomized, single-blind trial
  - 97 patients with CKD, treated with SPS for 3 days
  - Significant reduction in serum potassium
  - Significant rate of adverse effects (GI, increasing BP)
- Prospective, randomized, double-blind, placebo-controlled trial
  - 33 patients with CKD (mean eGFR ~20 mL/min/1.73 m^2; mean potassium ~5.2 mEq/L)
  - Short duration (7 days)
  - SPS greater reduction in serum potassium
  - Increased rate of adverse effects
  - Small sample size

Nasir K, et al. *J Ayub Med Coll Abbottadad*. 2014;26(4):455-458. Lepage L, et al. *Clin J Am Soc Nephrol*. 2015;10(12):2136-2142.

Incidence of Colonic Necrosis

- Retrospective study (n=752)
  - 0.3% overall incidence
  - No cases in control group (n=862)
- Retrospective cohort
  - 0.14% vs 0.07%
  - Preparation with 33% sorbitol
- Systematic review
  - 30 reports (58 cases)
    - 41 preparations with sorbitol
    - 17 preparations without sorbitol
- Retrospective chart review
  - 0.4% overall incidence



Gerstman BB, et al. *Am J Kid Dis*. 1992;20:159-161. Watson MA, et al. *Am J Kid Dis*. 2012;60:409-416. Harel Z, et al. *Am J Med*. 2013;126(3):264.e9-264-e24. Hagan AE, et al. *Clin Nephrol*. 2016;85:38-43.

SPS Drug Interactions

- Prescribers and patients should consider separating SPS dosing from other medications taken by mouth by at least 6 hours
  - Reduction in quetiapine levels
  - Reduction in lithium absorption
  - Reduction in iron absorption

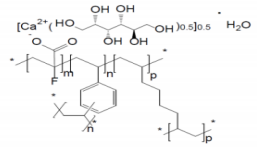
Hoge RH, et al. *J Clin Pharm Ther.* 2015;40(3):355-357. O'Connor TA, et al. *Ann Emerg Med*. 1996;28(5):504-507. US Food and Drug Administration (FDA) [website]. Drugs@FDA: FDA approved drug products. https://www.fda.gov/Drugs/DrugSafety/ucm468035.htm . Accessed May 18, 2018.

A patient is prescribed patiromer and asks about how long the product can be left out of a refrigerated environment. What is your response?

A. 1 week
B. 1 month
C. 3 months
D. Requires refrigeration

Organic Polymer Resin Patiromer Calcium Sorbitex (Patiromer; RLY5016)

- Potassium exchange resin
- Non-absorbed, non-degradable
- Primary effect in colon
- Powder packets
  - Specific instructions on preparing dose at home
  - Must be refrigerated, stable for 3 months at room temperature
  - **Take with or without food**
- Available as
  - 8.4 g, 16.8 g, 25.2 g powder packets
  - Once daily
  - Starting dose 8.4 g
  - Titrate weekly
  - Cost: $>700 per 30 packets in community, prices lower for hospitals



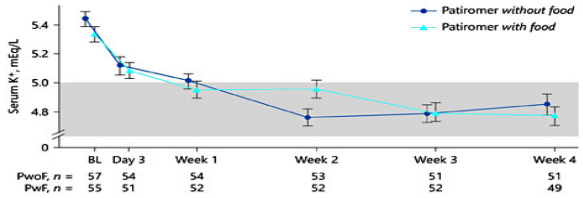
m = number of 2-fluoro-2-propenoate groups
n, p = number of crosslinking groups
H_2O = associated water
* = indicates an extended polymeric network

m = 0.91
n + p = 0.09

US Food and Drug Administration [website]. Drugs@FDA: FDA approved drug products. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&applno=205739. Accessed May 14, 2018.

Organic Polymer Resin Patiromer Calcium Sorbitex (Patiromer; RLY5016)

TOURMALINE Trial



- 87.3% of patiromer with food group and 82.5% of patiromer without food group achieved target potassium levels in the target range at either week 3 or week 4

Pergola PE, et al. *Am J Nephrol*. 2017;46:323-332. US Food and Drug Administration [website]. Drugs@FDA: FDA approved drug products. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&appIno=205739. Accessed May 14, 2018.

Patiromer Drug Interactions

- In vitro binding studies as part of FDA requirement
  - 28 drugs tested; 50% of drugs tested were bound by patiromer
  - Separate potential interacting drugs by 3 hours from patiromer

>50% Interaction	30%-50% Interaction	<30% Interaction
Amlodipine	Clopidogrel	Allopurinol
Cinacalcet	Lithium	Amoxicillin
Ciprofloxacin	Metoprolol	Apixaban
Levothyroxine	Verapamil	Aspirin
Quinidine	Warfarin	Atorvastatin
Trimethoprim		Cephalexin
		Digoxin
		Glipizide
		Lisinopril
		Phenytoin
		Rivaroxaban
		Spironolactone
		Valsartan

Drugs Evaluated
Amlodipine
Cinacalcet
Ciprofloxacin
Clopidogrel
Furosemide
Levothyroxine
Lithium
Metformin
Metoprolol
Trimethoprim
Verapamil
Warfarin

Department of Health and Human Services. Center for drug evaluation and research. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2015/205739Orig1s000RiskR.pdf. Weir MR, et al. *Kidney Int*. 2016;90:696-704.

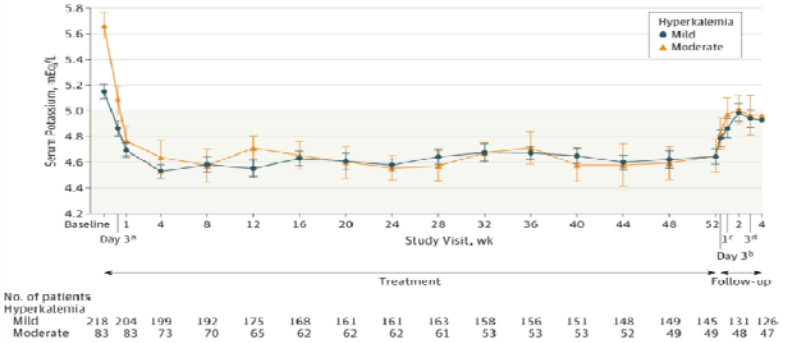
Patiromer Clinical Trial Data

Trial	Comments	Results
AMETHYST–DN 	• Dose finding, safety + efficacy • Diabetes mellitus + CKD (stages 3 and 4) • Hyperkalemic • Receiving RAASi • 52 weeks	• All patients on ACEI/ARB/combo • Majority on spironolactone • Effective for mild and moderate hyperkalemia • Serum K maintained for 52 weeks; increased 3 days after discontinuation
OPAL–HK 	• Safety + efficacy • CKD (stages 3 + 4) • Hyperkalemic • Receiving RAASi • 2 phases, 4 weeks + 8 weeks	• All patients on ACEI/ARB/combo • Effective for mild/mod/severe hyperkalemia • Constipation most common ADR (11%)
PEARL–HF 	• Safety, efficacy, tolerability • Chronic HF • Indication for spironolactone • Hyperkalemic • CKD + HF therapy (RAASi) • 4-week trial	• Incidence of hyperkalemia lower in treatment group • Additional benefit seen in those with CKD and HF • GI-related ADRs occurred in 21% of participants

ADR = adverse drug reaction.

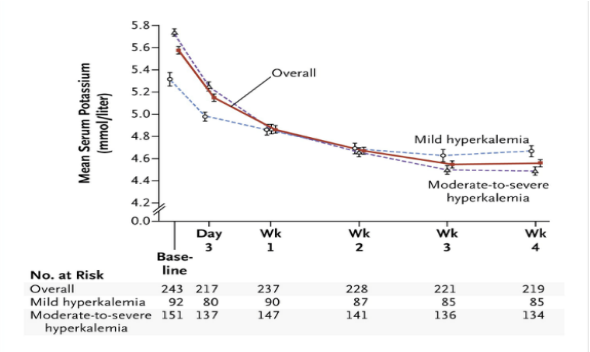
Bakris GL, et al. *JAMA*. 2015;314(2):151-161. Weir MR, et al. *N Engl J Med*. 2015;372:211-221.
Pitt B, et al. *Eur Heart J*. 2011;32(7):820-828.

AMETHYST-DN Trial: Serum Potassium Levels



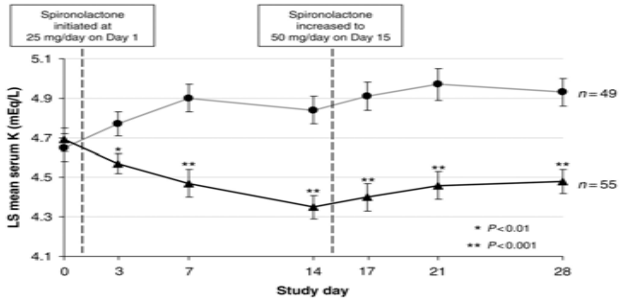
Bakris GL, et al. *JAMA*. 2015;314(2):151-161.

OPAL-HK Trial: Serum Potassium Levels



Weir MR, et al. *N Engl J Med*. 2015;372:211-221.

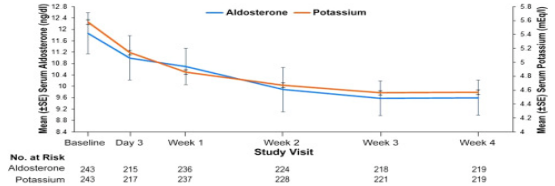
PEARL-HF Trial: Serum Potassium Levels



Pitt B, et al. *Eur Heart J*. 2011;32(7):820-828.

Additional Benefit of Patiromer

Measure	Mild Hyperkalemia	Mod/Severe Hyperkalemia	Overall
Serum aldosterone (ng/dL)	−1.81 ± 0.74	−3.19 ± 0.58	−2.50 ± 0.47
Systolic BP (mm Hg)	−5.40 ± 1.84	−5.57 ± 1.44	−5.48 ± 1.17
Diastolic BP (mm Hg)	−3.34 ± 1.21	−4.67 ± 0.95	−4.00 ± 0.77



Weir MR, et al. *Kidney Int*. 2016;90:696-704.

Patiromer: The Issues List

- Takes several hours for reduction in serum potassium
  - Onset occurs in 7 hours, full effect in days
- Questionable utility in emergent hyperkalemia
- Electrolyte disorders
  - Hypokalemia; hypomagnesemia
- Drug interactions
  - Metformin, levothyroxine, ciprofloxacin are most notable
  - Separate by at least 3 hours
- Higher cost
- Specific storage, mixing, and administration

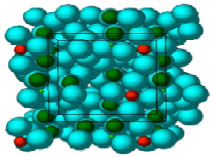
Pitt B, et al. *Expert Opin Drug Saf*. 2018;17(5):525-535.

A prescriber calls to ask about patiromer dosing and titration. What is the starting dose?

A. 8.4 g once daily
B. 8.4 g twice daily
C. 16.8 g once daily
D. 16.8 g twice daily

Update: FDA Approval of Sodium Zirconium Cyclosilicate (Formerly ZS-9)

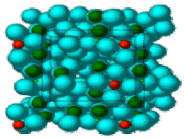
- May 21, 2018: FDA approves sodium zirconium cyclosilicate for oral suspension to treat adults with hyperkalemia
- Sodium zirconium cyclosilicate: Inorganic, non-absorbed, selective potassium ion trap

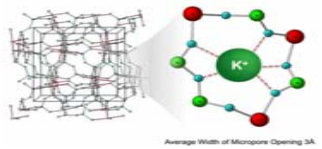


Stavros F, et al. *PLoS One*. 2014;9(12):e114686. US Food and Drug Administration. Drugs@FDA: FDA approved drug products. Sodium zirconium cyclosilicate. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&applno=20707.Accessed August 7, 2018.

Sodium Zirconium Cyclosilicate (Formerly ZS-9)

- Properties
  - Inorganic cation exchange resin
  - Non-absorbed, non-degradable
  - Crystalline lattice structure
  - Traps K+ throughout intestine
  - Exchanges Na+ and H+ for K+
- Available forms
  - Powder for suspension
  - Tablet, dissolvable?





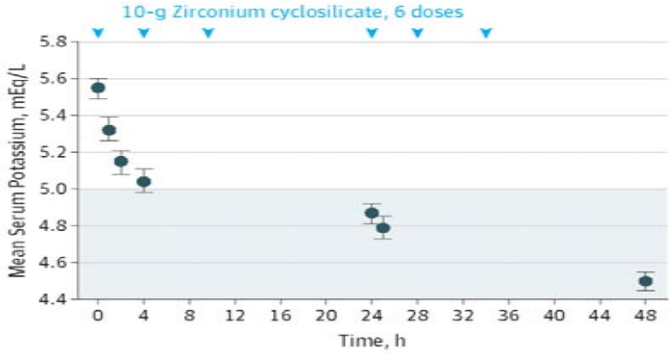
Stavros F, et al. *PLoS One*. 2014;9(12):e114686. US Food and Drug Administration. Drugs@FDA: FDA approved drug products. Sodium zirconium cyclosilicate. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&applno=20707.Accessed August 7, 2018.

HARMONIZE Trial

- Phase 3, randomized, double-blind, placebo-controlled trial
- Persistent hyperkalemia: Serum K+ >5.1 mEq/L
- 48-hour open-label phase
- Those achieving normokalemia randomized to 28-day study
  - Randomized to placebo or 3 different ZS-9* doses (5 g, 10 g, 15 g daily)
- 258 participants in initial 48-hour open-label phase
- 237 patients in 28-day study

*Former name of sodium zirconium cyclosilicate, which is now FDA approved.
HARMONIZE = Hyperkalemia Randomized Intervention Multi-Dose ZS-9 Maintenance.
Kosiborod M, et al. *JAMA*. 2014;312(21):2223-2233. Chaitman M, et al. *P&T®*. 2016;41(1):43-50.

HARMONIZE Trial



Kosiborod M, et al. *JAMA*. 2014;312(21):2223-2233.

HARMONIZE Trial

Kosiborod M, et al. *JAMA*. 2014;312(21):2223-2233.

HARMONIZE Trial

Adverse Effects	Open-Label Phase (10 g/d) N=258 No. (%)	Placebo N=85 No. (%)	ZS-9† 5 g N=45 No. (%)	ZS-9† 10 g N=51 No. (%)	ZS-9† 15 g N=56 No. (%)
Any event	20 (7.8)	27 (31.8)	24 (53.3)	15 (29.4)	25 (44.6)
Constipation	2 (0.8)	6 (7.1)	0	1 (2.0)	1 (1.8)
Edema*	0	2 (2.4)	1 (2.2)	3 (5.9)	8 (14.3)
Hypokalemia	0	0	0	5 (9.8)	6 (10.7)

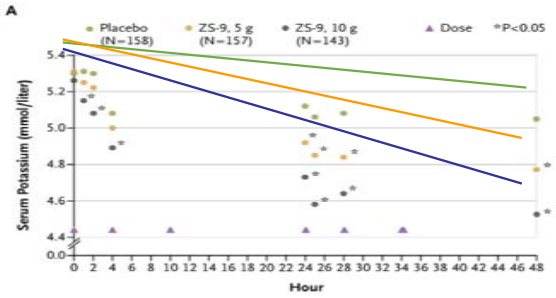
*Including generalized and peripheral edema. †Former name of sodium zirconium cyclosilicate, which is now FDA approved.
Kosiborod M, et al. *JAMA*. 2014;312(21):2223-2233.

ZS-9* in Hyperkalemia Trial

- Phase 3, randomized, two-stage, double-blind, placebo-controlled
- Stage 3 CKD
- Serum K, 5.0-6.5 mEq/L
- Dose-ranging study
- 753 patients randomized to receive ZS-9
  - 1.25 g, 2.5 g, 5 g, or 10 g
- 72% attained normal serum K
- Steepest decline in first 48 hours
- ADEs similar to those of placebo, primarily GI in nature

*Former name of sodium zirconium cyclosilicate, which is now FDA approved.
ADE = adverse drug event.
Packham DK, et al. *New Engl J Med*. 2015;372:222-231.

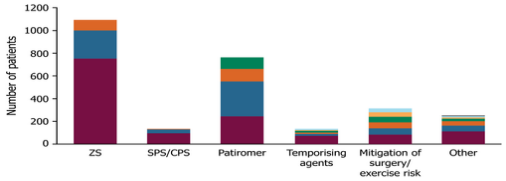
ZS-9* in Hyperkalemia Trial: Potassium Levels



*Former name of sodium zirconium cyclosilicate, which is now FDA approved.
Packham DK, et al. *New Engl J Med*. 2015;372:222-231.

Integration of New Binders into Clinical Practice

- Requires some effort for coverage by insurers
- Availability of product limited to specialty pharmacies and select community pharmacies
- Use in hospitals dependent on budget and formulary decisions
- Patiromer requires specific storage, mixing, and administration considerations
  - Now may be taken with or without food
  - Counseling important



Note: Each bar represents a treatment or a treatment category, with different colors representing separate studies within that category.

Palaka E, et al. *Int J Clin Pract*. 2018;72(2):e13052. Evidence in support of hyperkalemia management strategies: A systematic literature review. 2018;72(2). First published January 30, 2018. doi: 10.1111/ijcp.13052. http://www.4-traders.com/ASTRAZENECA-4000930/news/Study-Data-from-AstraZeneca-Update-Understanding-of-Hyperkalemia-Evidence-in-support-of-hyperkalaem-25958595/. Accessed May 14, 2018.

The Pharmacist's Role in the Management of Hyperkalemia

- Identify patients at risk for drug-induced hyperkalemia and opportunities to manage chronic conditions when at risk for hyperkalemia
- Counsel patients to ensure they have sufficient understanding, knowledge, and skill to follow their pharmacotherapeutic regimens and monitoring plans
- Seek ways to motivate patients to learn about their treatment and to be active partners in their care
- Liaise with dietitian regarding patients' diets to assess for sources of potassium

American Society of Health-System Pharmacists. ASHP guidelines on pharmacist-conducted patient education and counseling. *Am J Health-Syst Pharm*. 1997; 54:431-434. Raymond CB. *Can J Hosp Pharm*. 2013;66(6):369-374. Raymond CB, et al. *CANNT J*. 2010;20(3):49-54.

Lessons Learned

- SPS
  - Use limited by questionable efficacy and ADEs
- Patiromer
  - Effective for management of hyperkalemia
  - Use for emergency management of hyperkalemia not approved
  - ADEs are known and seem minimal
    - Primarily GI and hypomagnesemia
  - No serious ADEs
  - Low risk of drug–drug interactions with other oral medications
- Sodium zirconium cyclosilicate (formerly known as ZS-9)
  - Received FDA approval in May 2018 for the treatment of hyperkalemia in adults
  - No longer term studies
  - Appears effective for acute management

Conclusions

- Hyperkalemia is a common complication in patients with:
  - CKD and AKI
  - Diabetes mellitus
  - CVD
- Certain medications, such as RAASi, increase the risk of hyperkalemia
- SPS has questionable efficacy and safety concerns
- Newer agents, such as patiromer and sodium zirconium cyclosilicate:
  - Are more selective for potassium
  - Provide once-daily dosing
  - Require prior authorization for coverage

Questions?

Thank you for your attention!