LOKELMA is the leading branded K^+ binder in hospitals[1]

Once hyperkalemia develops among adult patients with risk factors, it may be a recurring problem*

WHAT IF YOU COULD RAPIDLY REDUCE AND SUSTAIN K^+ LEVELS OVER TIME?

INDICATION AND LIMITATION OF USE

LOKELMA is indicated for the treatment of hyperkalemia in adults.

LOKELMA should not be used as an emergency treatment for life-threatening hyperkalemia because of its delayed onset of action.

*Among patients with risk factors for hyperkalemia (HK) including chronic kidney disease, heart failure, diabetes, and use of renin-angiotensin-aldosterone system inhibitors, the risk of recurrence may increase. In a retrospective, claims-based analysis of 39,626 matched pairs of patients with or without HK, 40% of patients experienced 2 or more HK events during the 1-year post-index period. Patients with HK were defined as having 2 laboratory tests with a serum potassium level >5.0 mEq/L, at least 1 diagnosis code corresponding to HK (ICD-9 code 276.7), or at least 1 prescription fill of sodium polystyrene sulfonate. Most patients in this analysis had one or more HK risk factors.[2]

IMPORTANT SAFETY INFORMATION FOR LOKELMA® (sodium zirconium cyclosilicate)

WARNINGS AND PRECAUTIONS:

- **Gastrointestinal Adverse Events in Patients with Motility Disorders:** Avoid LOKELMA in patients with severe constipation, bowel obstruction or impaction, including abnormal post-operative bowel motility disorders. LOKELMA has not been studied in patients with these conditions and it may be ineffective and may worsen gastrointestinal conditions.
- **Edema:** Each 5-g dose of LOKELMA contains approximately 400 mg of sodium, but the extent of absorption by the patient is unknown. In clinical trials of LOKELMA in patients who were not on dialysis, edema was observed and was generally mild to moderate in severity and was more commonly seen in patients treated with 15 g once daily. Monitor for signs of edema, particularly in patients who should restrict their sodium intake or are prone to fluid overload (eg, heart failure or renal disease). Advise patients to adjust dietary sodium, if appropriate. Increase the dose of diuretics as needed.

  In a clinical trial of LOKELMA in patients on chronic hemodialysis in which most patients were treated with doses of 5 g to 10 g once daily on non-dialysis days, there was no difference in the mean change from baseline in interdialytic weight gain (a measure of fluid retention) between the LOKELMA and placebo groups.
- **Hypokalemia in Patients on Hemodialysis:** Patients on hemodialysis may be prone to acute illness that can increase the risk of hypokalemia on LOKELMA (eg, illnesses associated with decreased oral intake, diarrhea). Consider adjusting LOKELMA dose based on potassium levels in these settings.

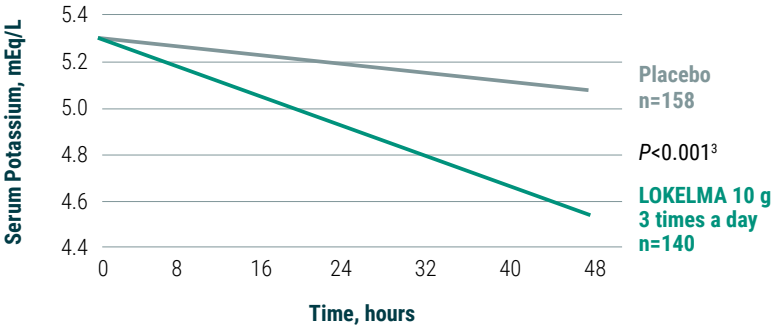
Please read additional Important Safety Information throughout and full Prescribing Information.

LOKELMA®
(sodium zirconium cyclosilicate)
5 g | 10 g for oral suspension

LOKELMA RAPIDLY REDUCED SERUM K^+ LEVELS

AND STARTED TO WORK IN AS EARLY AS 1 HOUR[3]

Primary Endpoint (Initial Phase): Exponential Rate of Change in Serum Potassium From Baseline to 48 Hours[3]



- In the initial phase of a multicenter, two-part, double-blind, randomized, placebo-controlled, Phase III trial, 753 patients received placebo or 1.25 g, 2.5 g, 5 g, or 10 g LOKELMA 3 times daily with meals for the initial 48 hours[4]
- Reductions in serum K^+ levels were observed 1 hour after initiation of therapy and continued to decline over the 48-hour treatment period with LOKELMA 10 g three times a day[3]
- The study met its primary endpoint, demonstrating a greater reduction in serum K^+ levels for patients receiving LOKELMA 10 g 3 times per day compared to placebo (P<0.001)[4]
- LOKELMA should not be used as an emergency treatment for life-threatening hyperkalemia because of its delayed onset of action
- For initial treatment of hyperkalemia, the recommended dose of LOKELMA is 10 g administered 3 times a day for up to 48 hours[4]
- LOKELMA was effective in lowering potassium levels in patients with chronic kidney disease, heart failure, diabetes mellitus, and those taking RAASi therapy[4]

IMPORTANT SAFETY INFORMATION (continued)

ADVERSE REACTIONS: The most common adverse reaction in non-dialysis patients with LOKELMA was mild to moderate edema. In placebo-controlled trials up to 28 days, edema was reported in 4.4%, 5.9%, 16.1% of non-dialysis patients treated with 5 g, 10 g, and 15 g of LOKELMA once daily, respectively vs 2.4% of non-dialysis patients receiving placebo.

DRUG INTERACTIONS: LOKELMA can transiently increase gastric pH. In general, oral medications with pH-dependent solubility should be administered at least 2 hours before or 2 hours after LOKELMA. Spacing is not needed if it has been determined the concomitant medication does not exhibit pH-dependent solubility.

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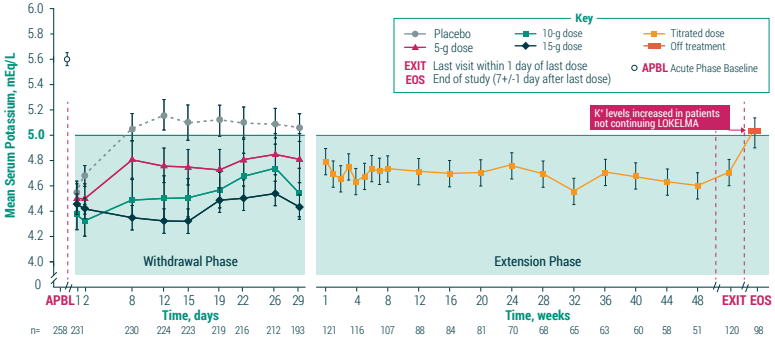
IN ANOTHER STUDY, LOKELMA HELPED PATIENTS ACHIEVE AND SUSTAIN NORMOKALEMIA* FOR UP TO 1 YEAR[4]

Mean Serum K+ Levels Through the Randomized Withdrawal and Extension Phases[4]



*Normokalemia=potassium range of 3.5 mEq/L to 5.0 mEq/L.

Double-blind randomized withdrawal phase[3]

- After the open-label initial phase of a multicenter, two-part, Phase III trial, in which 258 patients received 10 g LOKELMA administered 3 times daily with meals for 48 hours, patients who achieved a K+ level between 3.5 mEq/L and 5.0 mEq/L were randomized to receive 5 g, 10 g, or 15 g LOKELMA or placebo once daily, taken just before breakfast for 28 days in the withdrawal phase[4,5]
- Primary endpoint: All 3 doses of LOKELMA met the primary endpoint of lower mean serum potassium levels vs placebo over Days 8-29 ($P \leq 0.001$ for all doses)[4]

Extension phase[4]

- 123 patients who completed the withdrawal phase participated in the 11-month, open-label extension study[4]
- The treatment effect on serum K+ was maintained during continued therapy with LOKELMA for 11 months[4]
- The recommended maintenance dose is 10 g once daily. Monitor serum potassium and adjust the dose of LOKELMA at 1-week or longer increments of 5 g based on serum potassium level and desired target range. The recommended maintenance dose range is from 5 g every other day to 15 g daily[4]

IMPORTANT SAFETY INFORMATION (continued)

DOSING

- **Non-hemodialysis Patients**

  For initial treatment of hyperkalemia, the recommended starting dose is 10 g administered three times a day up to 48 hours. For maintenance treatment, the recommended starting dose is 10 g once daily. Monitor serum potassium and adjust dose of LOKELMA at 1-week intervals or longer in increments of 5 g based on serum potassium and desired target range. The recommended maintenance dose range is from 5 g every other day to 15 g daily. Discontinue or decrease the dose of LOKELMA if serum potassium is below the desired target range.

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5 g | 10 g for oral suspension

LOKELMA was shown to be safe and generally well tolerated[4]

- Safety was evaluated in clinical trials with **more than 1700 patients not on dialysis with hyperkalemia** and comorbidities including CKD (non-dialysis), DM, and CHF, in which a total of 507 patients were **treated for at least 1 year**[4]
- There are **no GI side effects** listed in the LOKELMA Prescribing Information; however, there were GI adverse events observed in the clinical studies[3-7]

Adverse events in non-dialysis patients

Edema

- In clinical trials of LOKELMA in patients who were not on dialysis, edema was generally mild to moderate in severity[4]
- In a placebo-controlled trial in which non-dialysis patients were treated with once-daily doses of LOKELMA for up to 28 days, edema was reported in 4.4%, 5.9%, and 16.1% of non-dialysis patients receiving 5 g, 10 g, and 15 g LOKELMA, respectively, compared with 2.4% of non-dialysis patients receiving placebo[4]
- In longer-term, uncontrolled trials, in which most non-dialysis patients were maintained on doses <15 g qd, edema (including edema, generalized edema, and peripheral edema) was reported in 8% to 11% of non-dialysis patients[4]
- In a pooled analysis of placebo-controlled trials in which non-dialysis patients were treated across all LOKELMA doses for up to 28 days, 0.2% of non-dialysis patients (1/479) discontinued LOKELMA due to edema[8]*

Hypokalemia

- 4.1% of LOKELMA-treated non-dialysis patients developed hypokalemia with a serum K^+ value <3.5 mEq/L, which resolved with dose reduction or discontinuation of LOKELMA[4]

*Edema, in the discontinuation rate analysis, includes generalized edema, peripheral edema, fluid overload, and fluid retention. During the maintenance phase, 1 patient who received 15 g LOKELMA qd was withdrawn due to general edema. There were no patient discontinuations due to edema for the initial phases of the trials.[8]

CHF=congestive heart failure; CKD=chronic kidney disease; DM=diabetes mellitus; GI=gastrointestinal; qd=once daily.

IMPORTANT SAFETY INFORMATION (continued)

DOSING (continued)

- **Hemodialysis Patients**

  For patients on chronic hemodialysis, administer LOKELMA only on non-dialysis days. The recommended starting dose is 5 g once daily on non-dialysis days. Consider a starting dose of 10 g once daily on non-dialysis days in patients with serum potassium greater than 6.5 mEq/L. Monitor serum potassium and adjust the dose of LOKELMA based on the pre-dialysis serum potassium value after the long interdialytic interval and desired target range. During initiation and after dose adjustment, assess serum potassium after one week. Discontinue or decrease the dose of LOKELMA if serum potassium falls below the desired target range based on pre-dialysis value after the long interdialytic interval or the patient develops clinically significant hypokalemia. The recommended maintenance dose range is from 5 g to 15 g once daily, on non-dialysis days.

Please read additional Important Safety Information throughout and full Prescribing Information.

You may report side effects related to AstraZeneca products by clicking here

References: 1. Data on file, US-41202, AZPLP. **2.** Betts KA, Woolley JM, Mu F, et al. The cost of hyperkalemia in the United States. *Kidney Int Rep*. 2017;3(2):385-393. **3.** Packham DK, Rasmussen HS, Lavin PT, et al. Sodium zirconium cyclosilicate in hyperkalemia [article and supplementary material]. *N Engl J Med*. 2015;372(3):222-231. **4.** LOKELMA® (sodium zirconium cyclosilicate) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2020. **5.** 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):2223-2233. **6.** Roger SD, Spinowitz BS, Lerma EV, et al. Efficacy and safety of sodium zirconium cyclosilicate for treatment of hyperkalemia: an 11-month open-label extension of HARMONIZE. *Am J Nephrol*. 2019;50(6):473-480. **7.** Spinowitz BS, Fishbane S, Pergola PE, et al. Sodium zirconium cyclosilicate among individuals with hyperkalemia: a 12-month phase 3 study. *Clin J Am Soc Nephrol*. 2019;14(6):798-809. **8.** U.S. Food & Drug Administration. Drug Approval Package: LOKELMA (sodium zirconium cyclosilicate) Medical Review(s). Accessed May 10, 2019. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2018/207078Orig1s000MedR.pdf

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