WHEN TREATING HYPERKALEMIA

GO WITH LOKELMA

CHOOSE THE PATH TO RAPID* AND SUSTAINED† K^+ CONTROL[1,2]

In a retrospective analysis of Study 3,

89% OF PATIENTS CONTINUED RAAS INHIBITOR USE‡[3]

*In Study 1, LOKELMA 10 g tid demonstrated a greater reduction in serum K^+ levels vs placebo at 48 hours ($P<0.001$) and started to work as early as 1 hour in patients with hyperkalemia not on dialysis.[1,2]

†In Study 2, patients with hyperkalemia who achieved normokalemia with LOKELMA in the 48-hour initial phase entered into the 28-day maintenance phase, where those who continued LOKELMA maintained lower mean serum K^+ levels vs those who switched to placebo, with a greater proportion of patients having mean serum K^+ in the normal range with LOKELMA vs placebo. Patients in Study 2 who continued into the open-label, 11-month extension phase sustained normokalemia with continued LOKELMA dosing.[1]

‡In a retrospective analysis of data from Study 3, 483 patients were receiving RAAS inhibitor at baseline. Of those patients, 74% maintained dose, 13% increased dose, 14% decreased dose, and 11% discontinued RAAS inhibitor use during the 12-month open-label trial. Patients were counted more than once if they required more than 1 RAAS inhibitor adjustment, so the total percentage across all 4 categories may exceed 100%.[3]

INDICATION AND LIMITATION OF USE

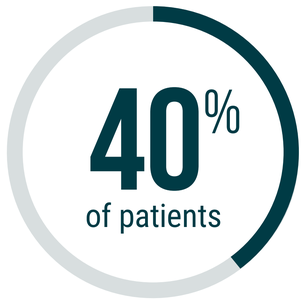
LOKELMA is indicated for the treatment of hyperkalemia in adults.

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

Please read additional Important Safety Information and full Prescribing Information by clicking buttons below.

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

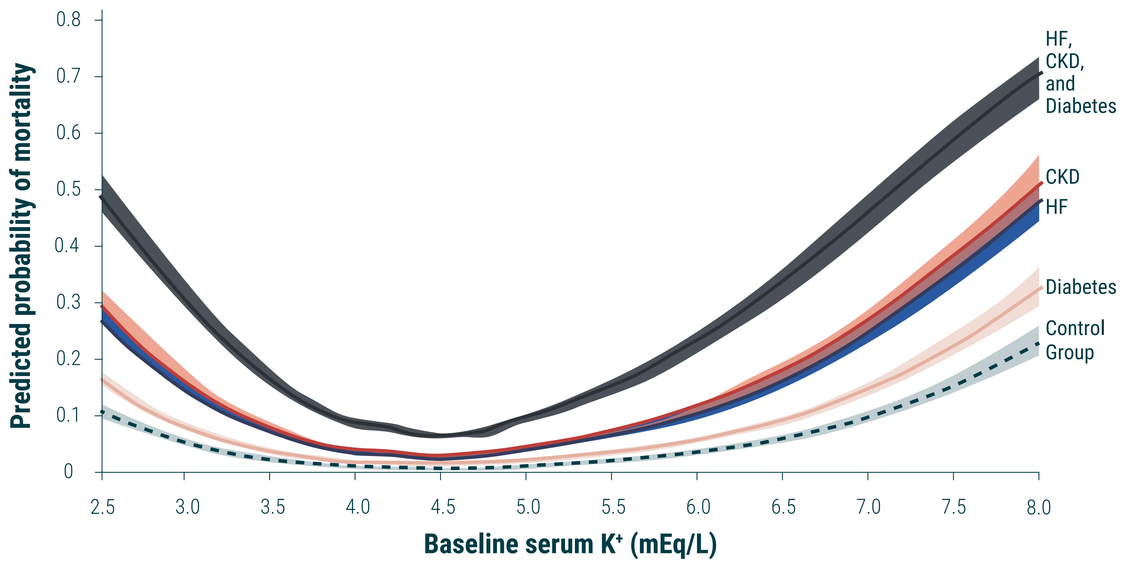
HYPERKALEMIA CAN BE A RECURRENT CONDITION AND POSES AN INCREASED RISK OF MORTALITY[4,5]



40% OF PATIENTS WITH HYPERKALEMIA EXPERIENCED 2 OR MORE HYPERKALEMIC EVENTS DURING THE 1-YEAR POST-INDEX PERIOD*[4]

- 15.6% of patients (n=6180) experienced ≥3 hyperkalemic events[4]
- 8.2% of patients (n=3234) experienced ≥4 hyperkalemic events[4]

In a study of almost 1 million patients, hyperkalemia was an independent risk factor for all-cause mortality†[5]



LOKELMA® (sodium zirconium cyclosilicate) is not indicated to reduce the risk of death.[1]

Serum K^+ ≥5.0 mEq/L was associated with an increased risk of all-cause mortality in patients with CKD, HF, diabetes, all 3, or none of these comorbidities.[5]

- Even mild hyperkalemia (5.0-<5.5 mEq/L) was associated with increased all-cause mortality over an average 18-month follow-up[5]

*Based on a retrospective analysis of a medical claims database with 39,626 matched pairs of patients with or without hyperkalemia.[6] Patients with hyperkalemia were defined as having 2 laboratory tests with a serum potassium level >5.0 mEq/L, at least 1 diagnosis code corresponding to hyperkalemia (ICD-9 code: 276.7), or at least 1 prescription fill of SPS.[6]

†Retrospective study of 911,698 patients from multiple integrated health delivery networks (Humedica). Control group included 338,297 individuals without known HF, CKD, diabetes, cardiovascular disease, or hypertension. Patient data came from private insurers, Medicare and Medicaid users, and uninsured individuals.[5]

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HOW WOULD YOU TREAT STEVEN'S HYPERKALEMIA?

STEVEN

63 years old

CKD Stage 4, hypertension, type 2 diabetes with recurrent hyperkalemia

"I'm worried about whether my current treatment plan will keep my potassium levels under control. I also struggle with maintaining a diet for my conditions."

- Previously prescribed SPS episodically to address recurrent hyperkalemic events, and recommended to dietitian for low-K^+ diet
- Experienced GI side effects from SPS
- Recent lab results show another hyperkalemia occurrence within 3 months, with a serum K^+ level of 5.7 mEq/L

PRESCRIBED LOKELMA:

Achieved and maintained normokalemia for 1 year with continued treatment—without the requirement of low-K^+ diet modification

Appreciated that LOKELMA is **tasteless and odorless**

Individual is a hypothetical patient, not an actual patient.

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REDUCING OR DISCONTINUING RAAS INHIBITOR THERAPY MAY NOT BE OPTIMAL FOR YOUR PATIENTS*[7]

THE KDIGO 2020 GUIDELINES FOR DIABETES MANAGEMENT IN CHRONIC KIDNEY DISEASE STATE[8]:

- In patients with diabetes, hypertension, and albuminuria, ACEi and ARB treatment should be initiated and titrated to the maximum approved dose that is tolerated[8]
- ACEi and ARB treatment should only be reduced or discontinued if serum K^+ levels cannot be otherwise managed[8]
- Recommendations to manage hyperkalemia include reviewing concurrent drugs, moderate K^+ intake, initiate diuretics or oral sodium bicarbonate in appropriate patients, and use of a gastrointestinal cation exchanger such as a K^+ binder[8]
- K^+ binders should be considered to decrease serum K^+ levels after other measures have failed, rather than decreasing or discontinuing ACEi and ARB treatment[8]

2x MORTALITY

MORTALITY WAS AT LEAST 2x HIGHER

for CKD patients whose RAAS inhibitor had been reduced or discontinued, compared to patients on maximum RAAS inhibitor doses.*[7]

*Based on data from an analysis of medical records for 66,862 patients with hyperkalemia† from the Humedica database. Patients with at least 1 outpatient RAAS inhibitor prescription were included in the 12-month analysis. Patients with end-stage renal disease, CKD stage 5, and acute kidney injury at the index date were excluded. Mortality‡ rates during the 12-month period were 4.1% for patients on maximum RAAS inhibitor dose, 8.2% for patients on submaximum dose, and 11.0% for patients who discontinued RAAS inhibitor therapy.[7]

†Hyperkalemia was defined as serum K^+ >5.0 mEq/L.[7]

‡Patients were categorized by their last RAAS inhibitor dose level for the analysis of mortality. Maximum was defined as the labeled dose and submaximum was defined as any dose lower than the labeled dose.[7]

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HOW WOULD YOU TREAT SOFIA'S HYPERKALEMIA?

SOFIA

58 years old

CKD Stage 3b, type 2 diabetes, hypertension with recurrent hyperkalemia

"It's difficult for me to manage all my conditions and dietary restrictions. I fear what might come next."

- Patient has difficulty adhering to low-K^+ diet in addition to diabetes diet
- Physician previously reduced her RAAS inhibitor dose to further manage her hyperkalemia
- Recent lab results show that patient is still hyperkalemic, with serum K^+ level 5.5 mEq/L

PRESCRIBED LOKELMA:

Achieved and maintained normokalemia for 1 year with continued use—without the requirement of low-K^+ diet modification

Guideline-recommended RAAS inhibitor use was reinitiated

Individual is a hypothetical patient, not an actual patient.

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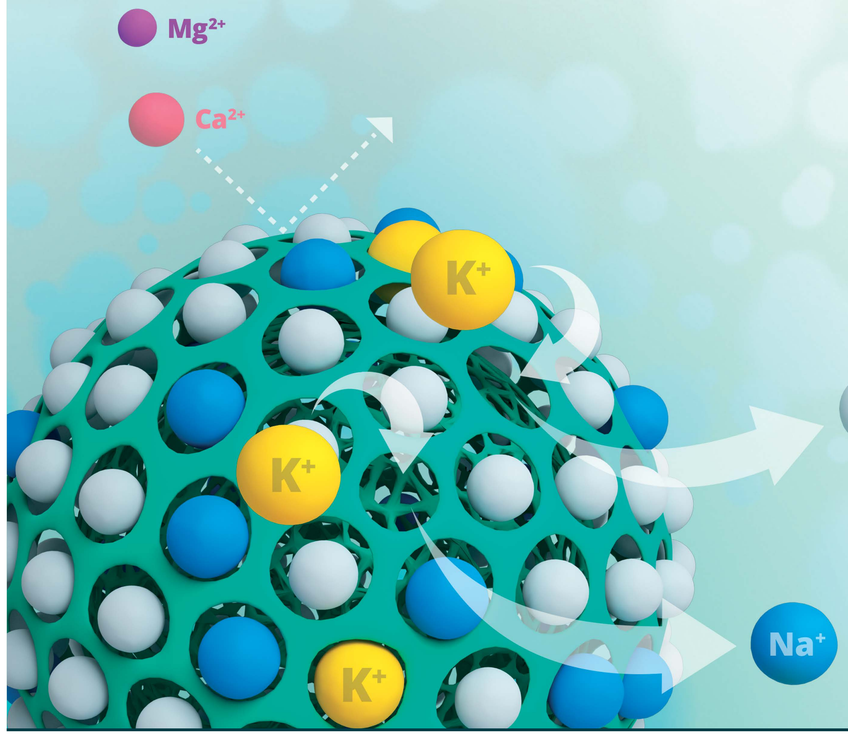
LOKELMA IS A HIGHLY SELECTIVE, INNOVATIVE K^+ BINDER[1]



LOKELMA is a modern K^+ binder that preferentially captures K^+ and exchanges it for hydrogen and sodium.[1,9]

LOKELMA has a unique crystal lattice structure.[9]

LOKELMA is insoluble and does not expand in water, so it is not expected to swell within the GI tract.[9]

For illustrative purposes only.

IMPORTANT SAFETY INFORMATION FOR LOKELMA

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.

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LOKELMA IS DIFFERENT THAN OTHER K^+ BINDERS[1,9]

	LOKELMA	SPS (sodium polystyrene sulfonate)*[10]	Veltassa® (patiromer) for oral suspension[11]
Selectivity	Binds K^+†[1]	Binds K^+, Ca^+, and Mg^+[10]	Binds K^+ and Mg^+[11]
Site of K^+ capture in lumen of GI tract	Small and large intestines‡[9]	Primarily large intestine[12]	Primarily colon§[12]
Time to initial K^+ reduction	1 hour[1]	Variable (hours to days)[10]	7 hours[11]
Longest duration studied prospectively	1 year[1]	7 days[13]	1 year[11]
Calcium content	0 g[14]	0 g[14]	1.6 g per 8.4 g of patiromer[15]
Sodium content for recommended maintenance dose range	400 mg qod-1200 mg daily‖[1]	1500 mg-6000 mg daily¶[16,17]	0[16,17]
Molecular composition	Non-polymer[13]	Polymer[13]	Polymer[13]

*Brand names for SPS include Kayexalate® and Kionex®.

†In vitro, LOKELMA has a high affinity for K^+, even in the presence of other cations such as calcium and magnesium.[1]

‡In vitro study; based on simulated intestinal fluid.[9]

§Based on nonclinical and early-phase studies.[18]

‖The sodium content/unit dose of LOKELMA is 400 mg/5 g, but the extent of absorption by the patient is unknown. The recommended maintenance dose range for patients not on dialysis is 5 g qod to 15 g daily (sodium content: 400 mg qod-1200 mg daily) and for patients on dialysis is 5 g to 15 g once daily, on non-dialysis days (sodium content: 400 mg-1200 mg daily on non-dialysis days).[1]

¶The sodium content/unit dose of SPS is 1500 mg/15 g. The in vivo efficiency of sodium-potassium exchange for SPS is approximately 33%; hence, about one-third of the actual sodium content is delivered to the body.[10] The recommended dose for SPS is 15 g 1 to 4 times daily.[10,16,17]

Clinical pharmacology does not correlate with efficacy or safety.

LIMITATION OF USE: LOKELMA should not be used as an emergency treatment for life-threatening hyperkalemia because of its delayed onset of action.[1]

LOKELMA causes a small dose-dependent increase in serum bicarbonate concentrations (1.1 mEq/L at 5 g once daily, 2.3 mEq/L at 10 g once daily and 2.6 mEq/L at 15 g once daily as compared with a mean increase of 0.6 mEq/L in patients treated with placebo). The clinical significance of this finding is unclear.[1]

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LOKELMA®
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5 g | 10 g for oral suspension

IN ADULT PATIENTS WITH HYPERKALEMIA WHO ARE NOT ON DIALYSIS,

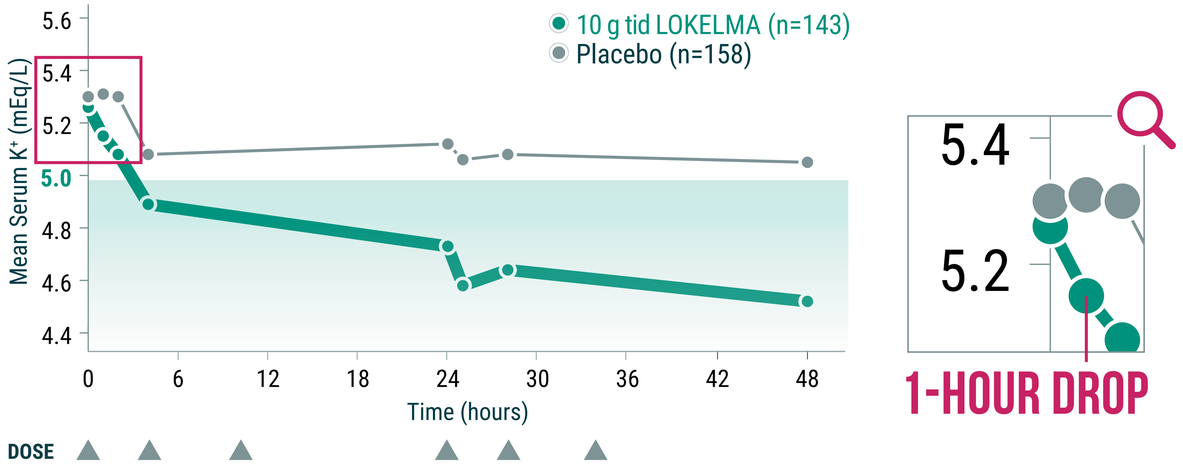
LOKELMA LED TO RAPID REDUCTION IN SERUM K^+ LEVELS IN AS EARLY AS 1 HOUR[1,2]

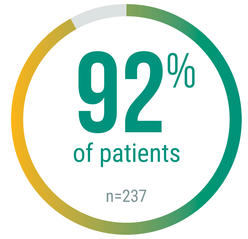
WORKS RAPIDLY

IN STUDY 1, within 1 hour after first dose of LOKELMA 10 g, reduction in K^+ levels was observed in patients[1,2]

The study met its primary endpoint demonstrating a greater reduction in serum K^+ levels over the **48-hour** initial treatment period with LOKELMA 10 g tid compared to placebo ($P<0.001$)[1,2]

STUDY 1: MEAN SERUM K^+ IN THE INITIAL PHASE OVER 48 HOURS[1,2]





IN STUDY 2, 92% of the patients enrolled (n=258) achieved normal K^+ levels within 48 hours from baseline[1]

- Average serum K^+ levels decreased from 5.6 mEq/L to 4.5 mEq/L (with LOKELMA 10 g tid for 48 hours)[1]

LIMITATION OF USE: LOKELMA should not be used as an emergency treatment for life-threatening hyperkalemia because of its delayed onset of action.[1]

STUDY 1 DESIGN: In the initial phase of a multicenter, 2-part, double-blind, randomized, placebo-controlled, phase 3 trial, 753 patients received placebo or 1.25 g, 2.5 g, 5 g, or 10 g LOKELMA tid for the initial 48 hours.[1,2]

STUDY 2 DESIGN: After the open-label initial phase of a multicenter, 2-part, phase 3 trial, in which 258 patients received 10 g LOKELMA tid for 48 hours, patients who achieved a K^+ level between 3.5 and 5.0 mEq/L were randomized to receive 5 g, 10 g, or 15 g LOKELMA or placebo once daily for 28 days in the maintenance phase. 123 patients who completed the maintenance phase participated in the 11-month, open-label extension study.[1,19]

IMPORTANT SAFETY INFORMATION FOR LOKELMA (cont'd)

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.

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5 g | 10 g for oral suspension

LOKELMA SUSTAINED NORMOKALEMIA* FOR UP TO 1 YEAR WITH CONTINUED TREATMENT[1]

SUSTAINS K^+

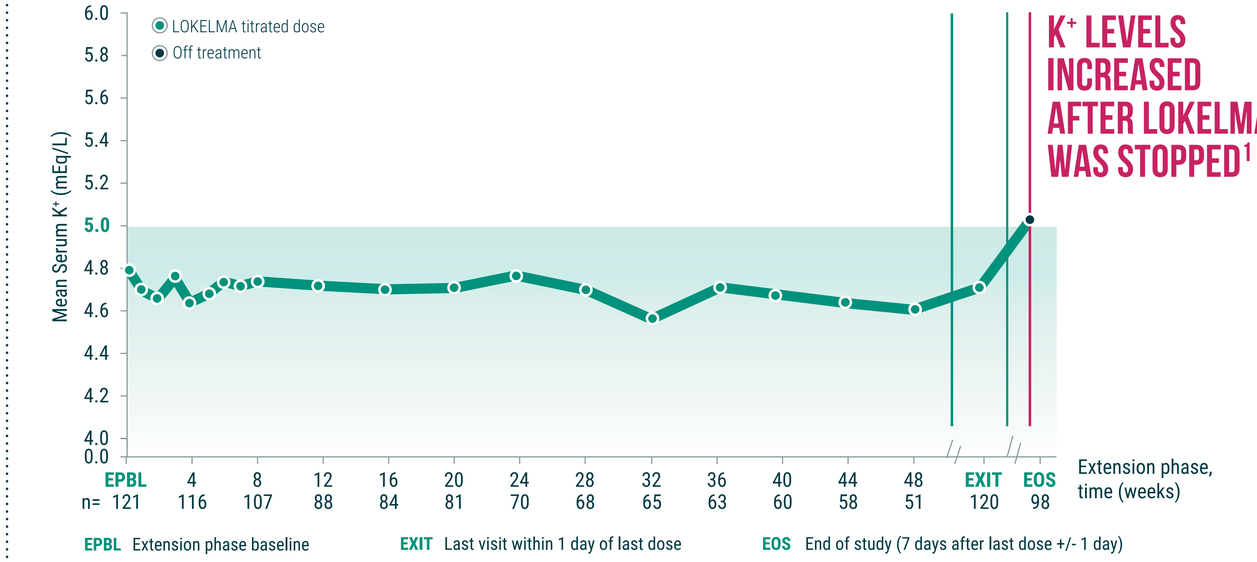
In STUDY 2 and STUDY 2 Extension, LOKELMA sustained normal serum K^+ levels for up to 1 year with continued treatment[1,19,20]

IN STUDY 2[1,19]:

- LOKELMA-treated patients (n=258) with hyperkalemia who achieved normokalemia at 48 hours were included in the double-blind, randomized maintenance phase of the study[1,19]
- Primary endpoint was met: mean serum K^+ levels on Days 8-29 were lower with LOKELMA 5 g, 10 g, and 15 g vs placebo (4.8 mEq/L, 4.5 mEq/L, and 4.4 mEq/L vs 5.1 mEq/L, respectively; $P \leq 0.001$ for all doses)[1,19]

STUDY 2 EXTENSION: In patients who remained in the open-label extension phase, LOKELMA sustained normal serum K^+ levels with continued treatment for 11 months[1]

MEAN SERUM K^+ LEVELS IN PATIENTS WHO COMPLETED A 28-DAY RANDOMIZED MAINTENANCE PHASE AND CONTINUED ON LOKELMA FOR 11 MONTHS[1]



- The mean dose of LOKELMA was 10 g qd in 73.2% (90/123) of patients; >10 g qd in 13.0% (16/123) of patients, and <10 g qd in 13.8% (17/123) of patients

STUDY 2 EXTENSION DESIGN: Patients who were included in the 28-day randomized maintenance phase of Study 2 had the option to continue treatment with LOKELMA in an open-label extension phase for up to 11 months (N=123). The LOKELMA dose was titrated in 5-g increments (to 5 g qod up to 15 g qd) based on i-STAT K^+ levels.[1,20]

*Normokalemia was defined as serum K^+ levels between 3.5 mEq/L and 5.0 mEq/L.[19,20]

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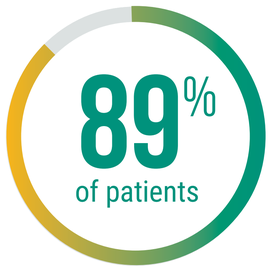
5 g | 10 g for oral suspension

IN A RETROSPECTIVE ANALYSIS OF STUDY 3,

A MAJORITY OF PATIENTS CONTINUED THEIR RAAS INHIBITOR USE*[3]



89% OF PATIENTS CONTINUED RAAS INHIBITOR USE WHILE TAKING LOKELMA†[3]

Among patients on RAAS inhibitor therapy (n=520) during the maintenance phase‡ of Study 3, a 12-month, open-label study evaluating LOKELMA in patients with hyperkalemia, 37 initiated therapy during the maintenance phase and 483 were on therapy at baseline. Of those 483 patients[3]:

- 74% of patients had no change in RAAS inhibitor therapy[3]
- 13% of patients had an increase in RAAS inhibitor dose§[3]
- 14% of patients had a decrease in RAAS inhibitor dose§[3]

Of the 263 patients who were RAAS inhibitor naive at baseline, 14% initiated RAAS inhibitor treatment during the study.

IN STUDY 3:

Over Months 3-12, mean serum K^+ ≤5.1 mEq/L was achieved by **88% of patients**.

→ **The treatment effect of LOKELMA was maintained with ongoing treatment regardless of RAAS inhibitor use[3]**

STUDY 3 DESIGN: LOKELMA was evaluated for long-term efficacy in 751 patients with hyperkalemia in an open-label, single-arm, 12-month, phase 3 study. Following the initial-phase treatment of LOKELMA 10 g tid, patients who achieved normokalemia‖ within 72 hours (n=746; 99%) entered the maintenance phase. For maintenance treatment, the initial dose of LOKELMA was 5 g qd and was adjusted to a minimum of 5 g qod up to a maximum of 15 g qd, based on i-STAT K^+ level. The primary endpoints included the percentage of patients who achieved normokalemia,‖ based on serum K^+ levels, during the initial phase and the percentage of patients who maintained mean serum K^+ ≤5.1 mEq/L during Months 3-12 of the maintenance phase.[1,3]

*Based on a retrospective analysis of the changes in RAAS inhibitor use during the maintenance phase of a 12-month, open-label study.[3]

†11% of patients receiving RAAS inhibitor at baseline (n=483) discontinued RAAS inhibitor during the 12-month open-label trial.[3]

‡Excluded 5 patients who discontinued RAAS inhibitor therapy prior to their first dose of the study drug.[3]

§Patients were counted more than once if they required more than 1 RAAS inhibitor adjustment, so the total percentage across all 4 categories may exceed 100%.[3]

‖Normokalemia was defined as K^+ levels between 3.5 mEq/L and 5.0 mEq/L.[1]

IMPORTANT SAFETY INFORMATION FOR LOKELMA (cont'd)

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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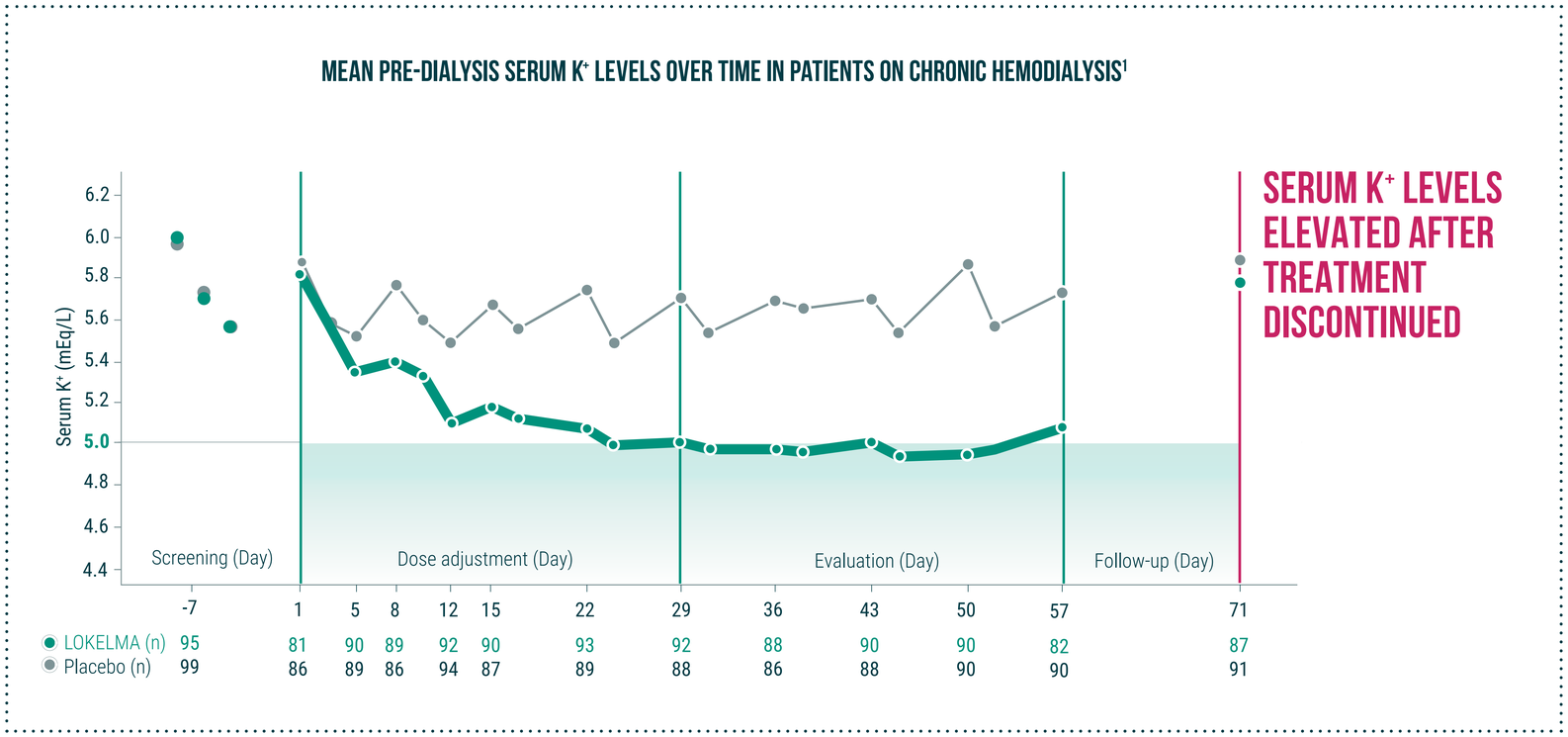
LOKELMA ACHIEVED AND SUSTAINED LOWER PRE-DIALYSIS K^+ LEVELS VS PLACEBO

LOKELMA IS THE ONLY FDA-APPROVED K^+ BINDER WITH EFFICACY AND SAFETY RESULTS IN THE LABEL FOR ADULT PATIENTS WITH HYPERKALEMIA ON CHRONIC HEMODIALYSIS[1]

STUDY 4:

- **41% of patients treated with LOKELMA (n=97) achieved the primary endpoint** compared to 1% of patients in the placebo group (n=99; *P*<0.001)
- Responders maintained pre-dialysis serum K^+ between 4.0-5.0 mEq/L during at least 3 of 4 hemodialysis treatments after the LIDI and did not receive rescue therapy* during the evaluation period

LOKELMA sustained lower pre-dialysis K^+ levels in patients on hemodialysis with continued treatment[1]



STUDY 4 DESIGN: DIALIZE was a double-blind, placebo-controlled trial in patients with end-stage renal disease on chronic hemodialysis (≥3 months) and persistent hyperkalemia† (n=196) who were randomized to receive LOKELMA 5 g or placebo once daily on non-dialysis days. In the initial 4-week period the dose could be adjusted weekly in 5-g increments up to 15 g qd on non-dialysis days to achieve pre-dialysis serum K^+ levels between 4.0 mEq/L and 5.0 mEq/L after the LIDI. The dose at the end of the dose-adjustment period was maintained throughout the 4-week evaluation period. Baseline mean pre-dialysis serum K^+ levels after the LIDI were 5.8 mEq/L in the LOKELMA group and 5.9 mEq/L in the placebo group.[1,21]

*Rescue therapy was defined as any urgent therapeutic intervention considered necessary to reduce serum K^+ in the setting of severe hyperkalemia (defined by protocol as >6.0 mEq/L). Rescue therapy use was left to the investigator's clinical judgment to be given in accordance with local practice guidelines.[21]

†Persistent hyperkalemia defined as pre-dialysis serum K^+ >5.4 mEq/L after the LIDI and >5.0 mEq/L after at least one SIDI.[21]

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IN STUDIES 1-3,

LOKELMA WAS SHOWN TO BE SAFE AND GENERALLY WELL TOLERATED[1]

Safety was evaluated in clinical trials with **more than 1700 patients not on dialysis with hyperkalemia** and comorbidities including CKD, DM, and CHF, with 507 patients **treated for at least 1 year**[1]

There are no **GI side effects** listed in the LOKELMA Prescribing Information; however, there were GI adverse events observed in the clinical studies[1,2,3,19,20]

94.1% of patients on the 10 g qd recommended maintenance dose **did not develop edema**[1]

95.9% of patients **did not develop hypokalemia**[1]

ADVERSE EVENTS IN PATIENTS NOT ON DIALYSIS

Edema

- In clinical trials of LOKELMA, edema was generally mild to moderate in severity[1]
- In placebo-controlled trials in which patients were treated with once-daily doses of LOKELMA for up to 28 days[1]:

LOKELMA			Placebo
5 g qd	10 g qd	15 g qd	
4.4%	5.9%	16.1%	2.4%

- 0.2% of patients (1/479) discontinued LOKELMA due to edema*[22]
- In longer-term, uncontrolled trials, in which most patients were maintained on doses <15 g qd, edema (including edema, generalized edema, and peripheral edema) was reported in 8% to 11% of patients[1]

Hypokalemia

- 4.1% of LOKELMA-treated patients developed hypokalemia with a serum K^+ value of <3.5 mEq/L, which resolved with dose reduction or discontinuation of LOKELMA[1]

*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.[22]

IMPORTANT SAFETY INFORMATION FOR LOKELMA

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.

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IN STUDY 4,

THE SAFETY OF LOKELMA WAS COMPARABLE TO PLACEBO FOR PATIENTS ON DIALYSIS[21]

OVERALL, 40 PATIENTS IN THE LOKELMA GROUP (41.7%) REPORTED ADVERSE EVENTS, COMPARED TO 46 PATIENTS IN THE PLACEBO GROUP (46.5%)[1,21]

	LOKELMA (n=97)	Placebo (n=99)
GI disorders	19.8%	17.2%
Infections	12.5%	9.1%
Overall SAEs	7.3%	8.1%

- In Study 4, 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**[1]

Hypokalemia

- 5% of patients developed pre-dialysis hypokalemia (serum K^+ <3.5 mEq/L) in both the LOKELMA and placebo groups; 3% and 1% of patients developed a serum K^+ <3.0 mEq/L in the LOKELMA and placebo groups, respectively[1]

Other Adverse Events

- The most common SAEs were angina pectoris (2.1%) in the LOKELMA group and hyperkalemia requiring rescue therapy (3%)* and fluid overload (2%) in the placebo group[21]
  - —None of the SAEs were related to study drug[21]

*Use of rescue therapy included but was not limited to insulin/glucose, sodium bicarbonate, β-adrenergic agonists, K^+ binders (sodium polystyrene sulfonate, calcium polystyrene sulfonate, patiromer), and any other form of renal replacement therapy including additional dialysis or reduction in dialysate K^+ concentration.[21]

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

DOSING FOR YOUR PATIENTS

DOSING FOR PATIENTS NOT ON DIALYSIS

RECOMMENDED STARTING DOSE

10 g
3X/DAY
FOR UP TO 48 HOURS

MAINTENANCE TREATMENT

10 g
1X/DAY
FOR UP TO 1 YEAR

- Monitor serum K^+ and adjust the dose of LOKELMA based on the serum K^+ level and desired target range[1]
- During maintenance treatment, up-titrate based on the serum K^+ level at intervals of 1 week or longer and in increments of 5 g[1]
- The recommended maintenance dose range is from 5 g qod to 15 g daily[1]
- Decrease the dose of LOKELMA or discontinue if the serum K^+ is below the desired target range[1]

DOSING FOR PATIENTS ON CHRONIC HEMODIALYSIS

MAINTENANCE TREATMENT

5 g
1X/DAY
ON NON-DIALYSIS DAYS

For patients on chronic hemodialysis, LOKELMA should only be dosed on non-dialysis days[1]

- The recommended starting dose is 5 g once daily on non-dialysis days[1]
- Consider a starting dose of 10 g once daily on non-dialysis days in patients with serum K^+ >6.5 mEq/L[1]
- Monitor serum K^+ and adjust the dose of LOKELMA based on the pre-dialysis serum K^+ value after the LIDI and desired target range[1]
- During initiation and after a dose adjustment, assess serum K^+ after 1 week[1]
- Recommended maintenance dose range is from 5 g to 15 g once daily, on non-dialysis days[1]
- Discontinue or decrease the dose of LOKELMA if:
  - —Serum K^+ falls below the desired target range based on the pre-dialysis value after the LIDI,[1] or
  - —The patient develops clinically significant hypokalemia[1]

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LOKELMA IS TASTELESS AND ODORLESS[1,19]

3 tbsp of water

HOW TO DOSE LOKELMA

- LOKELMA is a white to grey powder available as 5 g or 10 g foil-lined packet for oral suspension[1]
- Administer LOKELMA orally as a suspension in water[1]
- Empty the entire contents of the packet(s) into a drinking glass containing approximately 3 tablespoons of water or more, if desired[1]
- Stir well and drink immediately[1]
- If powder remains in the glass, add water, stir, and drink immediately. Repeat until no powder remains[1]

In general, other oral medications should be administered at least 2 hours before or 2 hours after taking LOKELMA.[1]

NON-DIALYSIS PATIENTS WERE NOT REQUIRED TO MAKE CHANGES IN POTASSIUM-LOWERING DIETS IN CLINICAL TRIALS[2,3,19,20]

- Advise patients to adjust dietary sodium, if appropriate[1]

Patients can take LOKELMA with or without food.[1]

No need to refrigerate LOKELMA.[1]

IMPORTANT SAFETY INFORMATION FOR LOKELMA (cont'd)

WARNINGS AND PRECAUTIONS (cont'd):

- **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.

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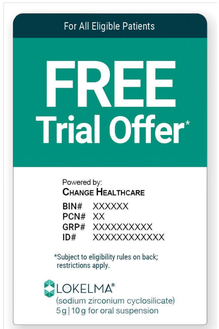
LOKELMA IS THE #1 PRESCRIBED BRANDED K^+ BINDER[1]

LOKELMA IS COVERED* FOR 87% OF COMMERCIAL AND MEDICARE PART D PATIENTS.†[2]

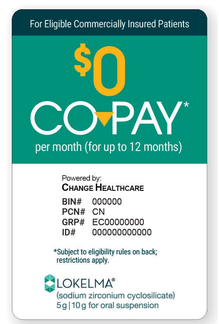
Complete Suite of Access and Affordability Services

My LOKELMA Support Program

- Assistance with understanding patient insurance coverage
- Prior authorization, claims, and appeal process support



- Free trial offer for all eligible patients‡
- Covers up to a 30-packet supply of LOKELMA



- Savings card for commercial patients§
- Reduces eligible patients' out-of-pocket costs to as low as $0 for up to 1 year

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*"Covered" is defined as any coverage level, specifically Tiers 1–7 and the $0 Co-pay Tier, regardless of restrictions.

†"Patients" is defined as covered lives Commercial, EGWP, Employer, Fed Prog, FEHBP, Medicare MA, Medicare PDP, Medicare SN, Medi-Medi, Municipal Plan, PACE, PBM, Union, at Tiers 1-7 in the nation, as calculated by Fingertip Formulary® as of 11/16/20.

Individual costs and benefit design may vary by plan. Please consult with individual plans for specific information. AstraZeneca does not endorse any Commercial, Medicare Part D, or Medicaid plan or plans.

‡Subject to eligibility rules. Restrictions apply.

§For commercially insured patients. Subject to eligibility. Restrictions apply.

References: 1. Data on file, US-41202, AZPLP. **2.** Formulary Data are provided by Fingertip Formulary® and are current as of 11/16/20.

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IMPORTANT SAFETY INFORMATION

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.

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.

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.

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Abbreviations: ACEi=angiotensin-converting enzyme inhibitor; AEs=adverse events; ARB=angiotensin II receptor blocker; CHF=congestive heart failure; CKD=chronic kidney disease; DM=diabetes mellitus; GI=gastrointestinal; HF=heart failure; K^+=potassium; KDIGO=Kidney Disease Improving Global Outcomes; LIDI=long interdialytic interval; qd=once daily; qod=every other day; RAAS=renin-angiotensin-aldosterone system; SAEs=serious adverse events; SIDI=short interdialytic interval; SPS=sodium polystyrene sulfonate; tid=3 times a day.

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WHEN TREATING HYPERKALEMIA

GO WITH LOKELMA

CHOOSE THE PATH TO RAPID* AND SUSTAINED† K^+ CONTROL[1,2]

In a retrospective analysis of Study 3,

89% OF PATIENTS CONTINUED RAAS INHIBITOR USE‡[3]

For patients not on dialysis

RAPID* REDUCTION[1,2]

Within 1 hour after first dose of LOKELMA 10 g, reduction in K^+ levels was observed in patients[1,2]

SUSTAINED† CONTROL[1]

The effect of LOKELMA was maintained for up to **1 year** with continued treatment[1]

GENERALLY WELL TOLERATED

The AEs listed in the LOKELMA label are edema and hypokalemia[1]

There are no GI side effects listed in the LOKELMA Prescribing Information; however, there were GI adverse events observed in the clinical studies[1,2,3,19,20]

ADVERSE REACTIONS REPORTED IN LOKELMA LABEL IN PATIENTS NOT ON DIALYSIS

Edema

- In clinical trials of LOKELMA, edema was generally mild to moderate in severity[1]
- In placebo-controlled trials in which 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 patients receiving 5 g, 10 g, and 15 g LOKELMA, respectively, compared with 2.4% of patients receiving placebo[1]
- In longer-term, uncontrolled trials, in which most patients were maintained on doses <15 g qd, edema (including edema, generalized edema, and peripheral edema) was reported in 8% to 11% of patients[1]
- In a pooled analysis of placebo-controlled trials in which patients were treated across all LOKELMA doses for up to 28 days, 0.2% of patients (1/479) discontinued LOKELMA due to edema§[22]

Hypokalemia

- 4.1% of LOKELMA-treated patients developed hypokalemia with a serum K^+ value <3.5 mEq/L, which resolved with dose reduction or discontinuation of LOKELMA[1]

*In Study 1, LOKELMA 10 g tid demonstrated a greater reduction in serum K^+ levels vs placebo at 48 hours (P<0.001) and started to work as early as 1 hour in patients with hyperkalemia not on dialysis.[1,2]

†In Study 2, patients with hyperkalemia who achieved normokalemia with LOKELMA in the 48-hour initial phase entered into the 28-day maintenance phase, where those who continued LOKELMA maintained lower mean serum K^+ levels vs those who switched to placebo, with a greater proportion of patients having mean serum K^+ in the normal range with LOKELMA vs placebo. Patients in Study 2 who continued into the open-label, 11-month extension phase sustained normokalemia with continued LOKELMA dosing.[1]

‡In a retrospective analysis of data from Study 3, 483 patients were receiving RAAS inhibitor at baseline. Of those patients, 74% maintained dose, 13% increased dose, 14% decreased dose, and 11% discontinued RAAS inhibitor use during the 12-month open-label trial. Patients were counted more than once if they required more than 1 RAAS inhibitor adjustment, so the total percentage across all 4 categories may exceed 100%.[3]

§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.[22]

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You are encouraged to report negative side effects of AstraZeneca prescription drugs by calling 1-800-236-9933. If you prefer to report these to the FDA, either visit www.FDA.gov/medwatch or call 1-800-FDA-1088.

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