

IN PATIENTS WITH HYPERKALEMIA NOT ON DIALYSIS, LOKELMA IS PRESCRIBED TO TREAT HK.¹ MANAGING HK CAN ENABLE GUIDELINE-RECOMMENDED RAASi TREATMENT²⁻⁴

In a prespecified exploratory analysis of Study 3⁵

NEARLY
9 OF 10
PATIENTS

continued RAASi therapy while taking LOKELMA long term.⁵

In the 483 patients on RAASi therapy at baseline, during the maintenance phase of Study 3, a 12-month, open-label study evaluating LOKELMA in patients with hyperkalemia:

- 74% of patients had no change in RAASi dose; 13% of patients had an increase in RAASi dose*; 14% of patients had a decrease in RAASi dose*; 11% of patients discontinued RAASi

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 (K⁺ = 3.5 - 5.0 mEq/L), 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.^{1,5} 89% of patients continued RAAS inhibitor use while taking LOKELMA.⁵

*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%.⁵

IMPORTANT SAFETY INFORMATION FOR LOKELMA

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.

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

- Diagnostic Tests:** LOKELMA has radio-opaque properties and, therefore, may give the appearance typical of an imaging agent during abdominal X-ray procedures

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.

Please read the full Important Safety Information on this spread and adjacent Brief Summary of full Prescribing Information.

Abbreviations: HK=hyperkalemia; K⁺=potassium; qd=once daily; qod=every other day; RAASi=renin-angiotensin-aldosterone system inhibitor; tid=3 times a day

References: 1. LOKELMA® (sodium zirconium cyclosilicate) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2022. 2. Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. *Kidney Int.* 2022;102(5S):S1-S127. doi:10.1016/j.kint.2022.06.008 3. Kidney Disease: Improving Global Outcomes (KDIGO) Blood Pressure Work Group. KDIGO 2021 clinical practice guideline for the management of blood pressure in chronic kidney disease. *Kidney Int.* 2021;99(3S):S1-S87. doi:10.1016/j.kint.2020.11.003 4. Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association joint committee on clinical practice guidelines. *J Am Coll Cardiol.* 2022;79(17):e263-e421. doi:10.1016/j.jacc.2021.12.012 5. 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. doi:10.2215/CJN.12651018

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

LOKELMA® (sodium zirconium cyclosilicate) for oral suspension

Brief Summary of Prescribing Information.

For complete prescribing information consult official package insert.

INDICATIONS AND USAGE

LOKELMA is indicated for the treatment of hyperkalemia in adults.

Limitation of Use

LOKELMA should not be used as an emergency treatment for life-threatening hyperkalemia because of its delayed onset of action [see *Clinical Pharmacology (12.2) and Clinical Studies (14) in the full Prescribing Information*].

DOSAGE AND ADMINISTRATION

Recommended Dosage

For initial treatment of hyperkalemia, the recommended dose of LOKELMA is 10 g administered three times a day for up to 48 hours. Administer LOKELMA orally as a suspension in water [see *Dosage and Administration (2.3) in the full Prescribing Information*].

For continued treatment, the recommended dose is 10 g once daily. Monitor serum potassium and adjust the dose of LOKELMA based on the serum potassium level and desired target range. During maintenance treatment, up-titrate based on the serum potassium level at intervals of 1-week or longer and in increments of 5 g. Decrease the dose of LOKELMA or discontinue if the serum potassium is below the desired target range. The recommended maintenance dose range is from 5 g every other day to 15 g daily.

Dosage Adjustment for Patients on Chronic Hemodialysis

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 inter-dialytic interval and desired target range.

During initiation and after a dose adjustment, assess serum potassium after one week. The recommended maintenance dose range is from 5 g to 15 g once daily, on non-dialysis days.

Discontinue or decrease the dose of LOKELMA if:

- serum potassium falls below the desired target range based on the pre-dialysis value after the long interdialytic interval, or;
- the patient develops clinically significant hypokalemia

Reconstitution and Administration

In general, other oral medications should be administered at least 2 hours before or 2 hours after LOKELMA [see *Drug Interactions (7) in the full Prescribing Information*].

Instruct patients to empty the entire contents of the packet(s) into a drinking glass containing approximately 3 tablespoons of water or more if desired. Stir well and drink immediately. If powder remains in the drinking glass, add water, stir and drink immediately. Repeat until no powder remains to ensure the entire dose is taken.

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

Gastrointestinal Adverse Events in Patients with Motility Disorders

Avoid use of LOKELMA in patients with severe constipation, bowel obstruction or impaction, including abnormal post-operative bowel motility disorders, because LOKELMA has not been studied in patients with these conditions and 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 (e.g., heart failure or renal disease). Advise patients to adjust dietary sodium, if appropriate. Increase the dose of diuretics as needed [see *Adverse Reactions (6) in the full Prescribing Information*].

In a clinical trial of LOKELMA in patients on chronic hemodialysis in which most patients were treated with doses of 5 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 (e.g., illnesses associated with decreased oral intake, diarrhea). Consider adjusting Lokelma dose based on potassium levels in these settings.

Diagnostic Tests

LOKELMA has radio-opaque properties and, therefore, may give the appearance typical of an imaging agent during abdominal X-ray procedures.

ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail elsewhere in the label:

- Edema [see *Warnings and Precautions (5.2) in the full Prescribing Information*].

Clinical Studies Experience

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

The total exposure to LOKELMA in the safety and efficacy clinical trials of patients not on dialysis with hyperkalemia was 1,760 patients with 652 patients exposed to LOKELMA for at least 6 months and 507 patients exposed for at least one year.

The population (n=1,009) in the placebo-controlled trials included patients aged 22 to 96 years, females (n=454), Caucasians (n=859) and Blacks (n=130). Patients had hyperkalemia in association with comorbid diseases such as chronic kidney disease, heart failure, and diabetes mellitus.

In placebo-controlled trials in which patients who were not on dialysis were treated with once daily doses of LOKELMA for up to 28 days, edema was reported in 4.4% of patients receiving 5 g, 5.9% of patients receiving 10 g and 16.1% of patients receiving 15 g LOKELMA compared to 2.4% of patients receiving placebo. In longer-term uncontrolled trials in which most patients were maintained on doses <15 g once daily, adverse reactions of edema (edema, generalized edema and peripheral edema) were reported in 8% to 11% of patients.

Laboratory Abnormalities

In clinical trials in patients who were not on dialysis, 4.1% of LOKELMA-treated patients developed hypokalemia with a serum potassium value less than 3.5 mEq/L, which resolved with dosage reduction or discontinuation of LOKELMA. In a clinical trial of LOKELMA in patients on chronic hemodialysis, 5% of patients developed pre-dialysis hypokalemia (serum potassium <3.5 mEq/L) in both the LOKELMA and placebo groups; 3% and 1% of patients developed a serum potassium < 3.0 mEq/L in the LOKELMA and placebo groups, respectively.

DRUG INTERACTIONS

LOKELMA can transiently increase gastric pH. As a result, LOKELMA can change the absorption of co-administered drugs that exhibit pH-dependent solubility, potentially leading to altered efficacy or safety of these drugs when taken close to the time LOKELMA is administered. In general, other oral medications should be administered at least 2 hours before or 2 hours after LOKELMA [see *Dosage and Administration (2.3) and Clinical Pharmacology (12.3) in the full Prescribing Information*]. LOKELMA is not expected to impact systemic exposure of drugs that do not exhibit pH-dependent solubility and so spacing is not needed if it has been determined that the concomitant medication does not exhibit pH-dependent solubility.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

LOKELMA is not absorbed systemically following oral administration and maternal use is not expected to result in fetal exposure to the drug.

Lactation

Risk Summary

LOKELMA is not absorbed systemically following oral administration, and breastfeeding is not expected to result in exposure of the child to LOKELMA.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

Geriatric Use

Of the total number of subjects in clinical studies of LOKELMA, 58% were age 65 and over, while 25% were 75 and over. No overall differences in safety or effectiveness were observed between these patients and younger patients.

PATIENT COUNSELING INFORMATION

Dosing

Instruct the patient how to reconstitute LOKELMA for administration. Inform the patient that it is necessary to drink the full dose [see *Dosage and Administration (2.3) in the full Prescribing Information*].

Instruct dialysis patients who experience acute illness (e.g., decreased oral intake of food or fluids, diarrhea) to contact the health care provider. The dose of LOKELMA may need to be adjusted [see *Warnings and Precautions (5.3) in the full Prescribing Information*].

Diagnostic Testing

Advise patients to notify their physician prior to an abdominal X-ray [see *Warnings and Precautions (5.4) in the full Prescribing Information*].

Drug Interactions

Advise patients who are taking other oral medications to separate dosing of LOKELMA by at least 2 hours (before or after) [see *Drug Interactions (7) in the full Prescribing Information*].

Diet

Advise patients to adjust dietary sodium, if appropriate [see *Warnings and Precautions (5.2) in the full Prescribing Information*].

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