# LOKELMA is the #1 prescribed branded $K^+$ binder[1]

Individual is a hypothetical patient, not an actual patient.

## LOKELMA PROVIDES RAPID* AND SUSTAINED† $K^+$ CONTROL FOR YOUR PATIENTS WITH HYPERKALEMIA[2,3]

*For patients not on dialysis:*

### RAPID*

**Started to work in as early as 1 hour[2,3]**

**LIMITATION OF USE:** LOKELMA should not be used as an emergency treatment for life-threatening hyperkalemia because of its delayed onset of action.[2]

### SUSTAINED[2†]

**Up to 1 year with continued treatment[2]**

### GENERALLY WELL TOLERATED[2]

- The AEs listed in the LOKELMA label were edema and hypokalemia[2]
- There are no GI side effects listed in the LOKELMA Prescribing Information; however, there were GI adverse events observed in the clinical studies[2-6]

### Adverse reactions reported in LOKELMA label in non-dialysis patients

**Edema**

- In clinical trials of LOKELMA, edema was generally mild to moderate in severity[2]
- 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[2]
- 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[2]
- 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[7†]

**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[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.

**Please see additional Important Safety Information on next page and full Prescribing Information.**

*In Study 1, LOKELMA 10 g tid demonstrated a greater reduction in serum $K^+$ levels vs placebo at 48 hours and started to work in as early as 1 hour in patients with hyperkalemia not on dialysis.[2,3]

In Study 2, LOKELMA-treated patients with hyperkalemia not on dialysis who achieved normokalemia at 48 hours maintained mean serum $K^+$ at lower levels than placebo at all 3 daily doses (5 g, 10 g, 15 g) in the 28-day randomized withdrawal phase. Patients in Study 2 who continued into the open-label, 11-month extension phase sustained normokalemia with continued LOKELMA dosing.[2]

†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.[7]

AEs=adverse events; GI=gastrointestinal; qd=once daily; tid=3 times a day.

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

US-39901 Expiration Date: 7/7/2021

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## IMPORTANT SAFETY INFORMATION FOR LOKELMA® (sodium zirconium cyclosilicate) (cont'd)

### WARNINGS AND PRECAUTIONS (cont'd):

- **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.

## 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.
- **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.

qd=once daily; qod=every other day.

**Please see additional Important Safety Information on previous page and full Prescribing Information.**

**References: 1.** Data on file, US-41202, AZPLP. **2.** LOKELMA® (sodium zirconium cyclosilicate) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2020. **3.** Packham DK, et al. Sodium zirconium cyclosilicate in hyperkalemia [article and supplementary material]. *N Engl J Med.* 2015;372(3):222-231. **4.** Kosiborod M, 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):2223-2333. **5.** Roger SD, 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. **6.** Spinowitz BS, 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. **7.** 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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