Drug Monograph

Drug/Drug Class:	**Lokelma™ (sodium zirconium cyclosilicate) for oral suspension / Potassium Lowering Electrolytes**
Prepared for:	MO HealthNet
Prepared by:	Conduent

☒ **New Criteria** ☐ **Revision of Existing Criteria**

Executive Summary

Purpose:	The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be made available on an open access basis to prescribers, require a clinical edit or require prior authorization for use.
Dosage Forms & Manufacturer:	Lokelma™ is available as a powder for oral suspension in 5 g and 10 g packets. Distributed by: AstraZeneca Pharmaceuticals LP, Wilmington, DE 19850.
Summary of Findings:	In a randomized, double-blind, two-part clinical trial (N=753), Lokelma™ showed improved serum potassium level concentrations versus placebo at both 48-hour and 12-day endpoints. Lokelma™ should be avoided in patients with gastrointestinal problems and edema should be monitored closely.

Status Recommendation:	☐ Prior Authorization (PA) Required ☐ Clinical Edit	☐ Open Access ☒ PDL
Type of PA Criteria:	☐ Increased Risk of ADE ☐ Appropriate Indications	☒ Under Solicitation ☐ No PA Required

Purpose

The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be considered a prior authorization drug, a clinical edit drug or an open access drug. While prescription expenditures are increasing at double-digit rates, payers are evaluating ways to control these costs by influencing prescriber behavior and guide appropriate medication usage. This review will assist in the achievement of qualitative and economic goals related to health care resource utilization. Restricting the use of certain medications can reduce costs by requiring documentation of appropriate indications for use, and where appropriate, encourage the use of less expensive agents within a drug class.

Introduction [2]

Hyperkalemia is defined at having a serum potassium level > 5-5.5 mEq/L in adults. Hyperkalemia can be a life threatening as it can lead to cardiac arrest or respiratory paralysis. Patients with hyperkalemia are often time asymptomatic and the disease is typically discovered through blood work. Determining the etiology of the hyperkalemia greatly impacts treatment options and severity of disease. There are a number of disease states and medications that can lead to reduced potassium excretion, increased intake, movement of potassium into extracellular space or a combination of these outcomes. It is important to determine the cause of the hyperkalemia in order to treat the patient comprehensively and to avoid potentially masking underlying diseases states.

Dosage Form(s) [1]

Lokelma™ is available as a powder for oral suspension in both 5 g and 10 g packets.

Manufacturer [1]

Distributed by: AstraZeneca Pharmaceuticals LP, Wilmington, DE 19850

Indication(s) [1]

Lokelma™ is indicated for the treatment of adults with hyperkalemia.

Clinical Efficacy [1] (mechanism of action/pharmacology, comparative efficacy)

Lokelma™ is a non-absorbed zirconium silicate that preferentially exchanges hydrogen and sodium for potassium. This exchange increases fecal potassium extraction as it binds to the potassium ions within the lumen on the gastrointestinal (GI) tract ultimately lowering serum potassium levels.

Pharmacokinetics:

	Lokelma™
Protein Binding	None
Volume of Distribution	Not systemically absorbed
Metabolism	None
Excretion	Feces
Half-life	Onset is 1 hour

Potassium Change from Baseline Study; 48 Hours Acute and 12 Day Maintenance

STUDY DESIGN	Two-part, double-blind, randomized, placebo-controlled clinical trial (N=753).
INCLUSION CRITERIA	Adult patients with hyperkalemia as defined as 5-6.5 mEq/L potassium level.
EXCLUSION CRITERIA	Patients that did not meet the inclusion criteria.
TREATMENT REGIMEN	Patients were randomized to receive one of 4 doses of Lokelma™ (1.25, 2.5, 5 or 10g) or placebo. The dose was given 3 times per day for the first 48 hours. The breakdown of patient dosing is as follows: Placebo (n=158), 1.25 mg (n=150), 2.5 mg (n=137), 5 mg (n=152) and 10 mg (n=140). The second part of the trial re-randomized the patients that were able to achieve a potassium level between 3.5 and 5 mEq/L after the acute dosing in the first part of the trial. These patients were given a once daily Lokelma™ dose (1.25, 2.5, 5, 10g) or placebo. The dose was given once daily with breakfast for 12 days.
RESULTS	The two-part clinical trial was able to meet the primary endpoints in both parts of the study. For the first part of the study, the acute dosing of three times per day showed a dose-dependent reduction of serum potassium levels throughout the different dosages. The 2.5, 5 and 10 g doses showed a greater reduction in serum potassium than compared to placebo. At 10 g three times per day (the recommended dosage of Lokelma™) showed a –0.7 mEq/L reduction in serum potassium over the 48 hours. It is important to note Lokelma™ was able to reduce serum potassium in patients with comorbidities, including chronic kidney disease, heart failure, diabetes and patients taking renin angiotensin aldosterone inhibitors. The second part of the trial showed a positive outcome for the maintenance phase of treatment compared to placebo. Over the 12-day treatment course, both the 5 and 10 g daily dose was able to show efficacy in maintaining serum potassium levels vs. placebo.
SAFETY	The most common side effect of mild to moderate severity edema. 4.1% of patients developed hypokalemia as defined by s serum potassium level < 3.5 mEq/L. All cases resolved with therapy discontinuation or a dose reduction.

Contraindications [1]

- There are no contraindications listed for Lokelma™.

Warnings and Precautions [1]

- Lokelma™ has a warning against GI adverse events in patients with motility disorders and should be avoided in patients with severe constipation. This also applies to patients with bowel obstruction or impaction and patients with abnormal post-operative bowel motility disorders.
- Lokelma™ should also be carefully monitored for edema as each 5 g dose contains approximately 400 mg of sodium. Signs and symptoms of edema should be monitored with all patients especially those with that are prone to fluid overload and/or already restricting sodium intake. It is important to advise patients they may need to adjust their dietary sodium intake in some cases.

Adverse Effects [1,3]*

Most common, ≥ 4%	**Lokelma™**	**Veltassa®**
Hypokalemia	4%	5%
Hypomagnesemia	NA	5-9%
Edema	4-16%	6%
Diarrhea	NA	5%
Constipation	NA	7%

**Adverse effects of sodium polystyrene sulfate are not defined.*

Drug Interactions [1]

- Lokelma™ does not have any known direct drug interactions, however the medication does increase gastric pH. This can lead to:
  - Altered absorption, efficacy and/or safety in medications with pH-dependent properties being co-administered with Lokelma™.
  - Lokelma™ is recommended to be given 2 hours before or 2 hours after other oral medications.

Dosage and Administration [1]

The FDA recommends a starting dose of 10 g three times per day for up to 48 hours for acute dosing. For maintenance dosing, the recommended dose is 10 g once daily. Dosage adjustments should be made in one-week intervals by 5 g daily to obtain target potassium serum range.

Cost

GENERIC NAME	BRAND NAME	MANUFACTURER	STRENGTH	DOSE	COST/DOSE*
Sodium polystyrene sulfate	Generic	KVK Tech	454 g bottle	15 g 1 – 4 times daily	$5.83
Patiromer	Veltassa®	Relypsa Inc	8.4 g packet	8.4 g daily	$32.83
Sodium zirconium cyclosilicate	Lokelma™	AstraZeneca	10 g packet	10 g daily**	$21.83

* Wholesale Acquisition Cost

**Maintenance Daily Dosage

Conclusion

Lokelma™ is a potassium binder available in oral powder form for the treatment of hyperkalemia in adult patients. In a two-part double-blind study (N=753), Lokelma™ showed decreased serum potassium levels in both acute (48-hour endpoint) and maintenance (12-day endpoint) dosing regimens versus placebo. The most common side effect during clinical trials include edema and hypokalemia. Due to the slow onset of action, Lokelma™ should not be used in emergency medicine for the treatment of hyperkalemia. For non-emergent hyperkalemia, treatment with Lokelma™ should not be used in patients with GI problems such as severe constipation, bowel obstruction, bowel impaction or abnormal bowel motility.

Recommendation

This drug is being considered for inclusion in the state specific Preferred Drug List (PDL).

References

1) Product Information: Lokelma™ (sodium zirconium cyclosilicate), AstraZeneca Pharmaceuticals LP, Wilmington, DE 19850 07/2018.
2) Lederer, Eleanor MD, Batuman, Vecihi MD et al. Hyperkalemia June 20, 2018 Medscape.
3) Online clinical reference Lexicomp “Veltassa” accessed November 1 2018.

Prepared by: Tyler Woods PharmD

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