Oscar Clinical Guideline: Lokelma (sodium zirconium cyclosilicate) (PG142, Ver. 1)

Lokelma (sodium zirconium cyclosilicate)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Hyperkalemia is a medical condition characterized by an abnormally high concentration of potassium (K+) in the blood. Normal serum potassium levels typically range between 3.5 and 5.0 millimoles per liter (mmol/L). Hyperkalemia is generally defined as a serum potassium level above 5.5 mmol/L. Elevated potassium levels can cause serious complications, including disturbances in cardiac conduction, muscle weakness, and, in severe cases, paralysis or fatal cardiac arrhythmias.

Hyperkalemia can result from various factors, including:

- Increased potassium intake: excessive consumption of potassium-rich foods or supplements.
- Decreased potassium excretion: reduced kidney function, certain medications (e.g., angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, potassium-sparing diuretics), and hormonal imbalances (e.g., adrenal insufficiency).
- Shifts in potassium distribution: movement of potassium from intracellular to extracellular space due to metabolic acidosis, tissue injury, or certain medications (e.g., beta-blockers, digoxin).

Hyperkalemia is typically diagnosed through laboratory tests, including blood tests to measure serum potassium levels and electrocardiogram (ECG) to assess for cardiac conduction abnormalities. The severity of hyperkalemia is commonly classified as follows:

1. Mild: Serum potassium levels of 5 (or upper limit of normal range) to 6 mEq/L without electrocardiogram (ECG) changes.
2. Moderate:
    a. Serum potassium levels of 5 (or upper limit of normal range) to 6 mEq/L with ECG changes.
    b. Serum potassium levels of 6.1 to 6.5 mEq/L without ECG changes.
3. Severe:
    a. Serum potassium levels of 6.1 to 6.5 mEq/L with ECG changes.
    b. Serum potassium levels of 6.5 mEq/L or higher.

Symptoms of hyperkalemia can be nonspecific and vary based on the severity and rate of onset. They may include:

- Weakness or fatigue
- Muscle cramps or pain
- Numbness or tingling sensations
- Nausea or vomiting
- Palpitations or irregular heartbeats
- Shortness of breath
- Chest pain

Treatment of hyperkalemia depends on the severity, underlying cause, and presence of any associated symptoms. Management strategies include:

- Discontinuing or adjusting medications that contribute to hyperkalemia.
- Dietary modifications to reduce potassium intake.
- Medical treatments aimed at promoting potassium excretion, such as diuretics, sodium polystyrene sulfonate (SPS), or patiromer.
- Intravenous calcium gluconate for acute stabilization of the cardiac membrane.
- Insulin and glucose administration to facilitate the movement of potassium into cells.
- Albuterol inhalation for mild cases, as it can help drive potassium back into cells.
- Dialysis in severe or refractory cases, particularly when kidney function is compromised.

LOKELMA® (sodium zirconium cyclosilicate) is a potassium binder indicated for the treatment of hyperkalemia in adults. It can be used for acute episodes of hyperkalemia, as well as for the chronic maintenance therapy to prevent the recurrence of hyperkalemia in patients at risk. LOKELMA® works by selectively binding to potassium ions in the gastrointestinal (GI) tract, particularly in the colon. This

binding helps to increase the excretion of potassium from the body through feces, thereby reducing the serum potassium levels.

Definitions

"Chronic kidney disease (CKD)" refers to a persistent anomaly in the structure or function of the kidneys, which lasts for a period of at least 3 months. It's identified by consistently unusual readings of real or approximated GFR (i.e., estimated GFR less than 60 mL/min/1.73 m^2) over a period of at least three months, or by instances where the GFR is within the normal range but irregularities are present in albuminuria levels, kidney biopsy results, or kidney imaging findings.

"**Dialysis**" is a medical procedure that removes waste products and excess fluid from the body when the kidneys are unable to do so effectively. There are two main types of dialysis: hemodialysis, which uses a machine to filter the blood externally, and peritoneal dialysis, which uses the lining of the abdomen to filter the blood internally.

"**ECG (Electrocardiogram)**" is a diagnostic test that records the electrical activity of the heart. It can detect abnormalities in heart rate, rhythm, and conduction, as well as indicate the presence of heart disease, heart attack, or electrolyte imbalances, such as hyperkalemia.

"**Hyperkalemia**" is a medical condition characterized by abnormally high levels of potassium (K+) in the blood. In adults, it is typically defined as a serum potassium concentration greater than 5.0-5.5 milliequivalents per liter (mEq/L), while the range in infants and children is age-dependent. Elevated potassium levels can lead to significant hemodynamic and neurologic consequences, with levels higher than 7 mEq/L considered life-threatening. Levels exceeding 8.5 mEq/L can cause respiratory paralysis or cardiac arrest and can quickly be fatal.

Medical Necessity Criteria for Initial Authorization

The Plan considers **Lokelma (sodium zirconium cyclosilicate)** medically necessary when **ALL** of the following criteria are met:

1. The medication is prescribed by or in consultation with a nephrologist **IF** there is documentation of **ANY** of the following:
    a. Hyperkalemia and chronic kidney disease; ***or***
    b. Unexplained hyperkalemia; ***AND***
2. The member is 18 years of age or older; ***AND***

3. The member has a diagnosis of hyperkalemia and documentation of **ONE** of the following:
    a. Acute hyperkalemia, if severe (or if moderate with ECG changes); ***or***
    b. The member's condition is characterized as **ONE** of the following and has tried and failed or is unable to use loop or thiazide diuretics due to contraindications, intolerability, or inadequate response:
        i. Acute hyperkalemia, if mild to moderate (and with no ECG changes); ***or***
        ii. Chronic hyperkalemia, and correctable causes have been identified and treated, but additional management of potassium levels is still required; ***or***
    c. Lokelma is being used as an adjunct therapy in combination with other treatments, such as diuretics, for acute or chronic hyperkalemia when the patient's condition warrants a multimodal approach to potassium management; ***AND***
4. The information reviewed does **NOT** indicate evidence of **ANY** of the following:
    a. the drug is being used as an emergency treatment for life-threatening hyperkalemia (i.e., at 7 to 8 mEq/L or higher); ***or***
    b. the member has severe constipation, bowel obstruction, or fecal impaction, including abnormal postoperative bowel motility disorders, unless corrected; ***or***
    c. Lokelma will be used in conjunction with another potassium binder (i.e., Patiromer, Sodium Polystyrene Sulfonate).

If the above prior authorization criteria is met, Lokelma (sodium zirconium cyclosilicate) will be approved for up to 3 months.

Medical Necessity Criteria for Reauthorization

Reauthorization for a six-month period will be approved if **BOTH** of the following are met:

1. Correctable causes of hyperkalemia have been identified and treated (e.g., dietary potassium restriction and/or discontinuation (or dose reduction) of medications contributing to hyperkalemia)***; AND***
2. Recent medical records (within the past three months) provide documented evidence of **BOTH** of the following:
    a. The member continues to require treatment for hyperkalemia to maintain safe potassium levels **OR** there is a high likelihood that serum potassium concentrations will increase without maintenance treatment***; and***
    b. The member has had a positive clinical response to therapy as evidenced by **ONE** of the following:

i. Reductions in elevated serum potassium concentrations from baseline***; or***

ii. Achievement of normokalemia (serum potassium concentration of 3.5–5 mEq/L).

Experimental or Investigational / Not Medically Necessary

Lokelma (sodium zirconium cyclosilicate) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. Non-covered indications include, but are not limited to:

- emergency treatment for life-threatening hyperkalemia because of its delayed onset of action.
- treating lithium toxicity.

Applicable Billing Codes

ICD-10 codes considered medically necessary if criteria are met:	
Code	*Description*
E87.5	Hyperkalemia

References

1. Batterink J et al: Pharmacological interventions for the acute management of hyperkalaemia in adults. Cochrane Database Syst Rev. 10:CD010344, 2015
2. Clase CM et al: Potassium homeostasis and management of dyskalemia in kidney diseases: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney Int. 97(1):42-61, 2020
3. Kosiborod M, Peacock WF, Packham DK. Sodium zirconium cyclosilicate for urgent therapy of severe hyperkalemia. N Engl J Med. 2015;372(16):1577-1578. doi:10.1056/NEJMc1500353
4. Kovesdy CP: Management of hyperkalemia: an update for the internist. Am J Med. 128(12):1281-7, 2015
5. Levin A et al. Kidney disease: improving global outcomes (KDIGO) CKD work group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Suppl. 2013;3(1):1-150.
6. Lokelma (sodium zirconium cyclosilicate) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; September 2022.
7. Moussavi K et al: Management of hyperkalemia with insulin and glucose: pearls for the emergency clinician. J Emerg Med. 57(1):36-42, 2019
8. Noel JA, Bota SE, Petrcich W, Garg AX, Carrero JJ, Harel Z, Tangri N, Clark EG, Komenda P, Sood MM. Risk of hospitalization for serious adverse gastrointestinal events associated with sodium polystyrene sulfonate use in patients of advanced age. JAMA Intern Med 2019.

9. Osborn MB: Potassium. In: Adams JG et al, eds: Emergency Medicine. 2nd ed. Elsevier; 2013:1397-404.e1
10. Packham DK, Rasmussen HS, Lavin PT, et al. Sodium zirconium cyclosilicate in hyperkalemia. N Engl J Med. 2015;372(3):222-231
11. Palmer BF, Carrero JJ, Clegg DJ, et al. Clinical management of hyperkalemia. Mayo Clin Proc. 2021;96(3):744-762. doi:10.1016/j.mayocp.2020.06.014
12. Peacock WF, Rafique Z, Vishnevskiy K, et al. Emergency potassium normalization treatment including sodium zirconium cyclosilicate: a phase II, randomized, double-blind, placebo-controlled study (ENERGIZE). Acad Emerg Med. 2020;27(6):475-486. doi:10.1111/acem.13954
13. Rossignol P et al: Emergency management of severe hyperkalemia: guideline for best practice and opportunities for the future. Pharmacol Res. 113(Pt A):585-91, 2016
14. Rossing P, Caramori ML, Chan JCN, Heerspink HJL, Hurst C, Khunti K, Liew A, Michos ED, Navaneethan SD, Olowu WA, Sadusky T, Tandon N, Tuttle KR, Wanner C, Wilkens KG, Zoungas S, Craig JC, Tunnicliffe DJ, Tonelli MA, Cheung M, Earley A, de Boer IH. Executive summary of the KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease: an update based on rapidly emerging new evidence. Kidney Int 2022;102;990-999.
15. Sterns RH et al: Treatment of hyperkalemia: something old, something new. Kidney Int. 89(3):546-54, 2016
16. Weir MR et al: Patiromer in patients with kidney disease and hyperkalemia receiving RAAS inhibitors. N Engl J Med. 372(3):211-21, 2015
17. Wong SWS et al: Polysulfonate resins in hyperkalemia: a systematic review. Can J Kidney Health Dis. 7:2054358120965838, 2020

Clinical Guideline Revision / History Information

Original Date: 06/01/2023
Reviewed/Revised: