Oxlumo (lumasiran)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the Oxlumo (lumasiran) drug policy is to ensure appropriate selection of patients for therapy based on product labeling, clinical guidelines, and clinical studies. The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Oxlumo (lumasiran) is indicated for the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary oxalate levels in pediatric and adult patients.

Limitations of Use

Oxlumo (lumasiran) is not approved for use in patients with or the treatment of primary hyperoxaluria type 2 (PH2) or type 3 (PH3) and is not expected to be effective because its mechanism of action does not affect the metabolic pathways causing hyperoxaluria in PH2 and PH3.

POLICY

Required Documentation

Submission of the following information is necessary to initiate the prior authorization review:

A. Initiation of therapy:
    1. Genetic testing or liver biopsy results confirming diagnosis
    2. Lab results confirming member has an estimated glomerular filtration rate (eGFR) greater than or equal to 30 mL/min/1.73m^2

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B. Continuation of therapy:
    1. Medical documentation of reduction in urinary oxalate excretion compared to baseline

Exclusion
Coverage will **not** be provided for members with any of the following:
- Primary hyperoxaluria type 2 or type 3
- History of renal or liver transplant
- Estimated glomerular filtration rate (eGFR) less than 30 mL/min/1.73m^2
- Members with clinical evidence of systemic oxalosis

Criteria for Initial Approval
A. Oxlumo (lumasiran) may be considered **medically necessary** for the treatment of primary hyperoxaluria type 1 (PH1) when all the following criteria are met:
    1. The member has a diagnosis of PH1 as confirmed by one of the following:
        a. Genetic testing demonstrating mutation in the alanine:glyoxylate aminotransferase (AGXT) gene
        b. Liver biopsy demonstrating significantly decreased or absent alanine:glyoxylate aminotransferase (AGT) enzyme activity
    2. The medication is prescribed by, or in consultation with, a nephrologist or another specialist experienced in the treatment of PH1
    3. The member is using in combination with high fluid intake
    4. The member is using in combination with pyridoxine OR has had a trial and inadequate response to pyridoxine

    Approval will be for **6 months**

Continuation of Therapy

A. Oxlumo (lumasiran) may be considered **medically necessary** for the continued treatment of primary hyperoxaluria type 1 (PH1) when all the following criteria are met:
    1. The member is receiving a positive clinical response to therapy from baseline as demonstrated by a reduction or maintained reduction in urinary oxalate excretion
    2. The member will continue using in combination with high fluid intake and pyridoxine (unless the member has had a trial and inadequate response to pyridoxine)
    3. The medication is prescribed by, or in consultation with, a nephrologist or another specialist experienced in the treatment of PH1

    Approval will be for **12 months**

Oxlumo (lumasiran) is considered **not medically necessary** for members who do not meet the criteria set forth above.

Dosage and Administration
Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

CLINICAL RATIONALE

Oxlumo (lumasiran), an RNA interference (RNAi) agent, is the first medication approved by the FDA for the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary oxalate levels in pediatric and adult patients. Oxlumo works by degrading HAO1 messenger RNA and reducing the synthesis of glycolate oxidase (GO), which inhibits hepatic production of oxalate. PH1 is a rare genetic disorder characterized by overproduction of oxalate and usually progresses to kidney failure. The estimated prevalence of PH1 is 1

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to 3 cases per 100,000 individuals in the general population. In the United States, less than 1,000 individuals have been diagnosed with PH, and PH1 accounts for 70% to 80% of patients diagnosed with PH.

The efficacy of Oxlumo was established in ILLUMINATE-A, a randomized, placebo controlled, double-blind study in 39 patients 6 years of age and older with PH1. Patients received 3 loading doses of 3 mg/kg Oxlumo or placebo administered once monthly, followed by quarterly maintenance doses of 3 mg/kg Oxlumo or placebo. The primary endpoint was the percent reduction from baseline in 24-hour urinary oxalate excretion corrected for body surface area (BSA) averaged over months 3 through 6. The least squares (LS) mean percent change from baseline in 24-hour urinary oxalate in the Oxlumo group was -65% vs. -12% in the placebo group (between-group LS mean difference of 53%, 95% CI: 45, 62; $p < 0.0001$). By month 6, 52% of patients treated with Oxlumo achieved a normal 24-hour urinary oxalate corrected for BSA vs. 0% placebo-treated patients ($p = 0.001$). Oxlumo was superior to placebo in reducing urinary oxalate excretion, plasma oxalate, and urinary oxalate to creatinine ratio over 6 months. There was no treatment effect on kidney stone events or kidney function.

In addition, the efficacy of Oxlumo was evaluated in ILLUMINATE-B, a single-arm study in 18 patients < 6 years of age with PH1. Efficacy analyses included the first 16 patients who received 6 months of treatment with Oxlumo and dosing was based on body weight. The primary endpoint was the percent reduction from baseline in spot urinary oxalate:creatinine ratio averaged over months 3 through 6. Patients treated with Oxlumo achieved a reduction in spot urinary oxalate:creatinine ratio from baseline of 71% (95% CI: 65, 77) over 6 months. Lower rates of renal stone events were seen after 6 months to 12 months of Oxlumo treatment. The most common adverse events that occurred were injection site reaction and abdominal pain.

The findings in ILLUMINATE-A and -B are mutually substantiating and provide substantial evidence of lumasiran's effectiveness in lowering urinary oxalate. Per the FDA's review, although it is difficult to translate the observed decreases in urinary oxalate to clinical benefit based on the available data, given the size of the treatment effect and knowledge of the pathophysiology of the disease, the findings are likely to translate to a benefit on important clinical manifestations of the disease, including nephrolithiasis and related complications, and loss of kidney function.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- J3490 Unclassified drugs
- J3590 Unclassified biologic drugs
- C9074 Injection, lumasiran, 0.5 mg (termed 7/1/2021)
- J0224 Injection, lumasiran, 0.5 mg (effective 7/1/2021)

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POLICY HISTORY

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