WellMed Doctors helping patients for more than 25 years	**Effective Date: 10/27/23**	**Revision Date(s):**
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Policy Number: 067.000

Title: Coverage Determination Policy for Oxlumo (lumasiran)

Regions: ☒ **Texas** ☐ **Florida** ☐ **Indiana** ☐ **New Jersey** ☒ **New Mexico**

Impacted Areas:

- ☒ Network Management/Provider Services
- ☐ Member services
- ☐ Quality Management
- ☐ Credentialing
- ☐ IT
- ☐ Administration
- ☐ Compliance/delegation
- ☒ Utilization Management
- ☐ Case management
- ☐ Disease management
- ☒ Claims
- ☐ Human resources
- ☐ Finance
- ☒ Pharmacy
- ☐ ALL

Available LCD/NCD/LCA: None

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Coverage Policy Number: 067.000

Line of Business: Medicare Part B

Policy Type: Prior Authorization

Coverage Determination:

Initial/New Requests

Oxlumo (lumasiran) is medically necessary for the treatment of **Primary Hyperoxaluria type 1 (PH1**) in patients who meet **ALL** of the following criteria:

A. Diagnosis of PH1 by, or in consultation with, a specialist (e.g., geneticist, nephrologist, urologist)

B. Confirmation of the PH1 diagnosis based on ALL of the following:

   I. Metabolic testing demonstration of **ONE** of the following:

      a. Increased urinary oxalate excretion (e.g. greater than 1 mmol/1.73 m2 per day [90 mg/1.73 m2 per day], increased urinary oxalate: creatinine ratio relative to normative values for age)

      b. Increased plasma oxalate and glyoxylate concentrations

   II. Genetic testing has confirmed a mutation in the alanine: glyoxylate aminotransferase (AGT or AGXT) gene

C. Patient has not received a liver transplant

D. Oxlumo is prescribed by, or in consultation with, a specialist (e.g., geneticist, nephrologist, urologist)

E. Oxlumo dosing is in accordance with the United States Food and Drug Administration approved labeling

F. Initial authorization will be for no more than 6 months.

Renewal/Continuation of Therapy Requests

For continuation of therapy request for Oxlumo, **ALL** of the following must be met:

A. Submission of medical records (e.g., chart notes, laboratory values) documenting a positive clinical response to therapy from pre-treatment baseline (e.g., decreased urinary oxalate concentrations, decreased urinary oxalate: creatinine ratio, decreased plasma oxalate concentrations)

B. Patient has not received a liver transplant

C. Oxlumo is prescribed by, or in consultation with, a specialist (e.g., geneticist, nephrologist, urologist)

D. Oxlumo dosing is in accordance with the United States Food and Drug Administration approved labeling

E. Reauthorization will be for no more than 12 months.

FDA Approved Dose and Indication

FDA Approved Indication	FDA Approved Dose
Primary hyperoxaluria, type I	Loading dosage: 3 mg/kg subQ once monthly for 3 months; Maintenance dosage: 3 mg/kg once every 3 months starting 1 month after last loading dose

General Background

PH1 is a rare genetic disease that causes the liver to over product oxalate; a waste product that is primarily removed by the kidneys through the urine due to mutations in the alanine glyoxylate aminotransferase (AGXT) gene. When the liver produces too much oxalate it can damage the kidneys by causing stones (nephrocalcinosis) and deposit in other organs causing injury and at times permanent damage.

Typical signs and symptoms or PH1 consist of kidney stones (nephrolithiasis), nephrocalcinosis, impaired kidney function, and systemic oxalosis (i.e bone disorders, cutaneous/vascular/cardiac/ophthalmologic/ and neurologic manifestations). In pediatric patients affected with PH1, impaired physical growth from infancy to early childhood is often seen because of impaired kidney function.

Oxalate a HAO1-directed small interfering ribonucleic acid (siRNA) which acts upstream of the metabolic defect in AGT to reduce oxalate production.

Diagnosis of PH1 typically consists of metabolic testing such as a 24-hour urine test and plasma oxalate measurement as well as genetic testing for AGXT mutations to confirm the diagnosis of PH1. There are 3 types of PH, however PH1 is the common type, accounting for 70-80% of PH cases[3]. Oxlumo is not expected to be effective in primary hyperoxaluria type 2 (PH2) or type 3 (PH3) because its mechanism of action does not affect the metabolic pathways causing hyperoxaluria in PH2 and PH3.

Clinical Evidence

ILLUMINATE-A was a randomized, double-blind trial comparing lumasiran and placebo in 39 patients 6 years of age and older with PH1 and an eGFR ≥ 30 mL/min/1.73 m2 (ILLUMINATE-A; NCT03681184). Patients received 3 loading doses of 3 mg/kg Oxlumo (N = 26) or placebo (N = 13) administered once monthly, followed by quarterly maintenance doses of 3 mg/kg Oxlumo or placebo [see Dosage and Administration (2.1)]. After six months, all patients received Oxlumo. The median age of patients at first dose was 15 years (range 6 to 61 years), 67% were male, and 77% were White. At baseline, the median 24-hour urinary oxalate excretion corrected for body surface area (BSA) was 1.7 mmol/24 h/1.73 m2 , the median plasma oxalate level was 13.1 µmol/L, 33% of patients had eGFR ≥ 90 mL/min/1.73 m2 , 49% had eGFR of 60 to < 90 mL/min/1.73 m2 , and 18% had eGFR 30 to < 60 mL/min/1.73 m2 , 56% were on pyridoxine, and 85% reported a history of symptomatic kidney stone events. The primary endpoint was the percent reduction from baseline in 24-hour urinary oxalate excretion corrected for BSA averaged over Months 3 through 6. The LS mean percent change from baseline in 24-hour urinary oxalate in the Oxlumo group was - 65% (95% CI: - 71, - 59) compared with - 12% (95% CI: - 20, - 4) in the placebo group, resulting in a between-group LS mean difference of 53% (95% CI: 45, 62; p < 0.0001)[3].

ILLUMINATE-B was a single-arm study in 18 patients 45 mL/min/1.73 m2 for patients ≥ 12 months of age or a normal serum creatinine for patients < 12 months of age (ILLUMINATE-B; NCT03905694). Dosing was based on body weight [see Dosage and Administration (2.1)]. The median age of patients at first dose was 51 months (range 4 to 74 months), 56% were female, and 88% were White. Three patients were less than 10 kg, 12 were 10 kg to < 20 kg, and 3 were ≥ 20 kg. The median spot urinary oxalate: creatinine ratio at baseline was 0.47 mmol/mmol. 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 72% (95% CI: 66, 78) (Figure 2). The reduction in urinary oxalate excretion was maintained with continued Oxlumo treatment through Month 12[4].

ILLUMINATE-C: A total of 21 patients were enrolled and treated with Oxlumo in a multi-center, single-arm study in patients with PH1 and an eGFR ≤ 45 mL/min/1.73 m2 in patients 12 months of age and older or an elevated serum creatinine for age in patients less than 12 months of age, including patients on hemodialysis. ILLUMINATE-C included 2 cohorts. Cohort A included 6 patients who did not require dialysis at the time of study enrollment. Cohort B included 15 patients who were on a stable regimen of hemodialysis; the hemodialysis regimen was to remain stable in these patients for the first 6 months of the study. Patients received the recommended dosing regimen of Oxlumo based on body weight [see Dosage and Administration (3.1)]. Patients requiring peritoneal dialysis were excluded. The median age of patients at first dose was 9 years (range 0 to 59 years), 57% were male, and 76% were White. For Cohort A, the median plasma oxalate level was 58 µmol/L. For Cohort B, the median pre-dialysis plasma oxalate level was 104 µmol/L. The primary endpoint was the percent change in plasma oxalate from baseline to Month 6 (average from Month 3 to Month 6) for Cohort A (N =

6) and the percent change in pre-dialysis plasma oxalate from baseline to Month 6 (average from Month 3 to Month 6) for Cohort B (N = 15). The percent change from baseline to Month 6 in plasma oxalate levels in Cohort A was an LS mean difference of -33% (95% CI: -82, 15) and in Cohort B was -42% (95% CI: -51, -34). Mean plasma oxalate decreased from 65 µmol/L (95% CI: 21, 108) at baseline to 33 µmol/L (95% CI: 10, 56) at Month 6 in Cohort A, and from 108 µmol/L (95% CI: 92, 125) at baseline to 62 µmol/L (95% CI: 51, 72) at Month 6 in Cohort B[5].

HCPCS Code

HCPCS Code	J0224: lumasiran, 0.5 mg
Available Dosage Form (s)	94.5mg/0.5mL single dose vial
Route of Administration	Subcutaneous, to be administered by a healthcare professional only

Acronyms

PH1 = Primary hyperoxaluria type 1

PH2 = Primary hyperoxaluria type 2

PH3 = Primary hyperoxaluria type 3

Si-RNA = Small interfering ribonucleic acid

AUA = American Urological Association

AGXT = Alanine glyoxylate aminotransferase gene

AGT = Alanine glyoxylate aminotransferase

HAOI = Hydroxyacid oxidase 1

PH = Primary hyperoxaluria

References

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4. A Study to Evaluate Lumasiran in Children and Adults With Primary Hyperoxaluria Type 1 (ILLUMINATE-A). Clinicaltrials.gov website https://clinicaltrials.gov/ct2/show/NCT03681184?term=lumasiran&draw=2&rank=4. Accessed December 1, 2020.
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