09-J3000-91

Original Effective Date: 03/15/21

Reviewed: 11/09/22

Revised: 12/15/22

Subject: Lumasiran (Oxlumo) injection

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Primary hyperoxaluria type 1 (PH1) is a metabolic disorder that causes the overproduction of oxalate. Calcium oxalate crystals form in the kidneys and result in recurrent nephrolithiasis, nephrocalcinosis, and progressively leads to renal dysfunction. Plasma accumulation of oxalate occurs as renal function declines and may cause damage to other organs (e.g., retina, myocardium, blood vessels, bone).

PH1 is caused by a autosomal recessive genetic mutation of the AGXT gene which results in dysfunction of the liver enzyme alanine:glyoxylate aminotransferase (AGT). The deficient AGT enzyme results in the conversion of glyoxylate to oxalate. AGT is a pyridoxal dependent enzyme and approximately 30-50% of patients may respond to pyridoxine treatment. A greater than 30% reduction in urine oxalate excretion after a minimum of 3 months of maximal pyridoxine (5 to 20 mg/kg/day) is considered a response. Other treatment options include reducing the formation of crystals in the urine through hyperhydration and urine alkalization with potassium citrate or sodium citrate. As disease progresses, dialysis may be necessary to remove excess plasma oxalate until liver transplant can occur.

Lumasiran (Oxlumo) is FDA approved for the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary and plasma oxalate levels in pediatric and adult patients. Through hepatocyte hydroxyacid oxidase 1 (*HAO1)* messenger ribonucleic acid (mRNA) interference, lumasiran reduces levels of glyoxylate oxidase (GO). This decreases the amount of available glyoxylate, a substrate for oxalate production. The GO enzyme is upstream of the AGT enzyme and independent of the underlying *AGXT* gene mutation. Lumasiran is not expected to be effective in primary hyperoxaluria type 2 (PH2) or type 3 (PH3) because these types of PH are caused by a different metabolic pathway.

The efficacy of lumasiran was demonstrated in two small clinical trials. In study 1, 39 patients were randomized to receive lumasiran or placebo. The patients had an estimated glomerular filtration rate of greater than or equal to 30 mL/min/1.73 m2, the median age was 15 years (range 6 to 61 years), 56% of patients were on pyridoxine, and 85% of patients had a history of symptomatic kidney stone events. The

primary endpoint was percent reduction from baseline in 24-hour urinary oxalate excretion corrected for BSA averaged over Months 3 through 6. There was a least squares mean percent decrease of -65% (95% CI: -71, -59) for the patients treated with lumasiran compared with -12% (95% CI: -20,-4) for placebo (between-group least squares mean difference 53% (95%CI: 45,62; p<0.0001). In study 2, 18 patients less than 6 years of age were evaluated in a single-arm study. The patients had an estimated glomerular filtration rate of greater than or equal to 45 mL/min/1.73 m2 if greater than or equal to 1 year of age or a normal serum creatinine for patient less than 1 year. The primary endpoint was percent reduction in spot urinary oxalate: creatinine ratio averaged over Months 3 through 6. Patients receiving lumasiran had a reduction in spot urinary oxalate:creatine ratio from baseline of 71% (95% CI: 65, 77). The most common adverse reaction was mild injection site reactions (e.g. erythema, pain, pruritus, swelling) and abdominal pain.

POSITION STATEMENT:

Initiation of lumasiran (Oxlumo) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Member is diagnosed with primary hyperoxaluria type 1 (PH1) confirmed by **ONE** of the following – documentation must be provided:
    a. Presence of a pathogenic AGXT gene mutation
    b. Liver biopsy demonstrates an alanine-glyoxylate aminotransferase (AGT) enzyme deficieny
2. Member demonstrates **ONE** of the following – documentation must be provided:
    a. Elevated 24 hour urine oxalate excretion corrected for body surface area (BSA) greater than the upper limit of normal (ULN)
    b. Elevated spot urine oxalate:creatinine ratio greater than the age-specific ULN
    c. Elevated plasma oxalate concentration greater than the ULN
3. **ONE** of the following:
    a. The member had an inadequate response to pyridoxine (i.e., ≤30% decrease in urine oxalate after 3 months of treatment with maximally tolerated pyridoxine)
    b. The member has a contraindication or intolerance to pyridoxine
    c. The member will receive treatment in combination with pyridoxine
4. Member has an inadequate response to or is not a candidate for urinary alkalization (i.e., potassium citrate or sodium citrate)
5. Member does not have primary hyperoxaluria type 2 or primary hyperoxaluria type 3
6. Member has not previously had a liver transplant
7. Lumasiran is prescribed by or in consultation with a nephrologist, urologist, hepatologist, gastroenterologist, or geneticist
8. The dose does not exceed weight based dosing in Table 1.

Approval duration: 6 months

Continuation of lumasiran (Oxlumo) **meets the definition of medical necessity** for the treatment of primary hyperoxaluria type 1 when **ALL** of the following criteria are met:

1. An authorization or reauthorization for lumasiran has been previously approved by Florida Blue or another health plan in the past 2 years for the treatment of primary hyperoxaluria type 1 (if another health plan, documentation of a health plan-paid claim for lumasiran during the 90 days immediately before the authorization request must be provided), **OR** the member has previously met **ALL** indication-specific criteria.
2. The member had a beneficial response to treatment (e.g., reduction of urine oxalate excretion or plasma oxalate levels from baseline) – documentation must be submitted
3. Member does not have primary hyperoxaluria type 2 or primary hyperoxaluria type 3
4. Member has not previously had a liver transplant
5. Lumasiran is prescribed by or in consultation with a nephrologist, urologist, hepatologist, gastroenterologist, or geneticist
6. The dose does not exceed weight based dosing in Table 1.

Approval duration: 12 months

Table 1. Dosing of Lumasiran (Oxlumo)

Body Weight	Loading Dose	Maintenance Dose (begin 1 month after the last loading dose)
Less than 10 kg	6 mg/kg once monthly for 3 doses	3 mg/kg once monthly
10 kg to less than 20 kg	6 mg/kg once monthly for 3 doses	6 mg/kg once every 3 months (quarterly)
20 kg and above	3 mg/kg once monthly for 3 doses	3 mg/kg once every 3 months (quarterly)

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

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

Dosing is based on actual body weight and consists of loading doses followed by maintenance doses.

Body Weight	Loading Dose	Maintenance Dose (begin 1 month after the last loading dose)
Less than 10 kg	6 mg/kg once monthly for 3 doses	3 mg/kg once monthly
10 kg to less than 20 kg	6 mg/kg once monthly for 3 doses	6 mg/kg once every 3 months (quarterly)
20 kg and above	3 mg/kg once monthly for 3 doses	3 mg/kg once every 3 months (quarterly)

If a dose is delayed or missed, administer as soon as possible. Resume prescribed monthly or quarterly dosing, from the most recently administered dose.

Administer after hemodialysis if administered on dialysis days.

Administer subcutaneous injection into the abdomen, thigh, or the side or back of the upper arms.

Rotate injection sites. Do not inject into scar tissue or areas that are reddened, inflamed, or swollen.

- If injecting into the abdomen, avoid the area around the navel.
- If more than one injection is needed for a single dose, the injection sites should be at least 2 cm apart.

Drug Availability

- Single-dose vials of 94.5 mg/0.5 mL

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- None

Precautions/Warnings

- None

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J0224	Injection, lumasiran, 0.5 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

E72.53	Primary hyperoxaluria

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 11/09/22.

GUIDELINE UPDATE INFORMATION:

03/15/21	New Medical Coverage Guideline.

04/01/21	Revision: Added HCPCS code C9074.
07/01/21	Revision: Added HCPCS code J0224 and deleted codes C9074 and J3490.
04/15/22	Review and revision to guideline; consisting of updating references.
12/15/22	Revision to guideline; consisting of updating the FDA approved use and dosing to include dialysis administration.