BlueCross BlueShield Nebraska

HYPEROXALURIA (PREAUTHORIZATION REQUIRED)

X.165

X.165 HYPEROXALURIA (PREAUTHORIZATION REQUIRED)

Target Agent

Oxlumo (lumasiran)

Objective: The intent of the lumasiran prior authorization is to encourage appropriate use according to clinical trial data and FDA approved labeling.

Dates

Original Effective
02-10-2021
Last Review
11-06-2024
Next Review
11-10-2025

POLICY

Prior Authorization Criteria for Approval:

1. Lumasiran (Oxlumo) will be considered **medically necessary** for the treatment of primary hyperoxaluria type 1 (PH1) when the following criteria are met:
   a. Information has been provided that indicates the patient has been treated with the requested agent starting on samples is not approvable) within the past 90 days **OR**
   b. The prescriber states the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days AND is at risk if therapy is changed **OR**
   c. Individual meets at least **ONE** of the following:

crystals in any biological fluid or tissue, increase serum creatinine with calcium oxylate (CaOx) stones, CaOx tissue deposits, renal failure of unknown causes, etc.); **OR**

ii. Individual does not have signs or symptoms but does have a family history of genetically confirmed PH

AND

a. One of the following:
   i. Individual has genetic testing indication homozygosity or compound heterozygosity for known mutations of AGXT **OR**
   ii. Liver biopsy demonstrates absent or significantly reduced alanine;glyoxylate aminotransferase (AGT) activity **AND**
b. Individual has **ONE** of the following:
   i. Urine oxylate (UOx) greater than the upper limit of normal **OR**
   ii. UOx/creatinine (CR) greater than the normal for age

AND

a. Individual has not had or is not scheduled for a liver and/or kidney transplant **AND**
b. Patient not currently treated with hemodialysis
c. Lumasiran (Oxlumo) is prescribed by or in consultation with a nephrologist or other healthcare provider experienced in treating PH1 **AND**
d. One of the following:
   i. Patient has tried and had inadequate response to potassium citrate or sodium citrate OR
   ii. Patient has intolerance or hypersensitivity to potassium citrate or sodium citrate OR
   iii. Patient has FDA labeled contraindication to BOTH potassium citrate and sodium citrate.

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)

Table 1. OXLUMO Weight-Based Dosing Regimen

Renewal criteria:

1. The Lumasiran (Oxlumo) will be renewed for **medical necessity** when ALL of the following criteria are met:
   a. Individual is diagnosed with PH1 **AND**
   b. Individual has reduced signs and symptoms of PH1 with lumasiran (Oxlumo) treatment **AND**
   c. Individual's laboratory values have improved or normalized **AND**
   d. Lumasiran (Oxlumo) is prescribed by or in consultation with a nephrologist or other healthcare provider experienced in treating PH1

Renewal length of approval: 12 months

*Lumasiran (Oxlumo) for any other indication is considered experimental/investigational and therefore non-covered. Scientific evidence does not support its use for any other indication.

DESCRIPTION

The primary hyperoxalurias are rare autosomal recessive inborn errors of metabolism of which three have been described at the molecular level. Primary hyperoxaluria type 1 (PH1) results from mutations in the *AGXT* gene with associated dysfunction of the vitamin B6 (pyridoxine)- dependent liver-specific peroxisomal enzyme alanine:glyoxylate aminotransferase (AGT).[3] The disorder results in overproduction and excessive urinary excretion of oxalate, causing recurrent urolithiasis and nephrocalcinosis. As glomerular filtration rate declines due to progressive renal involvement, oxalate accumulates leading to systemic oxalosis.[2] Long-term consequences include cardiomyopathy, cardiac conduction disturbances, vasculopathy, heart block, treatment resistant anemia, oxalate osteopathy resulting in debilitating bone and joint pain, retinopathy and if untreated, early death.[4]

The first sign or symptom is usually blood in the urine, pain, passage of a stone, or urinary tract infection. Patients with renal failure due to "infantile oxalosis" present with failure to thrive, anemia and acidosis. The majority of patients are symptomatic early in life and mostly before 10 years of age.[4]

The usual biochemical indicator of PH1 is a persistently and markedly elevated urine oxalate (UOx) excretion in the absence of secondary causes of hyperoxaluria. Once a raised urinary oxalate has been identified, the diagnosis is confirmed through genetic testing for mutation in the *AGXT* gene OR liver biopsy indicating deficiency of AGT enzyme activity.[2-4]

recommended to reduce urinary calcium oxalate precipitation thus decreasing stone growth or nephrocalcinosis.[2-4]

It may be replaced by sodium citrate appropriate to GFR and plasma potassium.[2,4] Pyridoxine (vitamin B6) is a co-factor for AGT and the administration of pyridoxine has been associated with a decrease in urine oxalate in about 30% of PH1 patients. Guidelines recommend that all patients receive administration of pyridoxine for a test period of a minimum of 3 months.[2-4] For those patients who are responsive (defined as a >30% decrease in urine oxalate), pyridoxine should be continued indefinitely or until liver transplantation.[2,4]

Oxlumo is a HAO1-directed small interfering ribonucleic acid (siRNA) indicated for the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary oxalate levels in pediatric and adult patients.

Lumasiran reduces levels of glycolate oxidase (GO) enzyme by targeting the hydroxyacid oxidase 1 (HAO1) messenger ribonucleic acid (mRNA) in hepatocytes through RNA interference. Decreased GO enzyme levels reduce the amount of available glyoxylate, a substrate for oxalate production. As the GO enzyme is upstream of the deficient alanine:glyoxylate aminotransferase (AGT) enzyme that causes PH1, the mechanism of action of lumasiran is independent of the underlying AGXT gene mutation. 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.

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. At baseline, 56% of patients were on pyridoxine (stable regimen for at least 3 months). 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% compared with -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 ($p = 0.001$).

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

Safety

Contraindications to lumasiran include:

- None

Lumasiran contains the following Black Box Warnings:

- None

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REFERENCES

2012
Cochat P, Hulton SA, Acquaviva C, et al. Primary Hyperoxaluria Type 1: Indications for Screening and Guidance for Diagnosis and Treatment. *Nephrol Dial Transplant*. 2012;27:1729-1736.

2016
Hulton SA. The Primary Hyperoxalurias: A Practical Approach to Diagnosis and Treatment. *Int J Surg*. 2016 Dec;36(D):649-654.

2009
Hoppe B, Beck BB, Milliner D. The Primary Hyperoxalurias. *Kidney Int*. 2009 Jun;75(12):1264-1271.

REVISIONS

12-05-2023
Policy reviewed at Medical Policy Committee meeting on 11/8/2023 – no changes to policy

06-25-2021
Added new code for 07/01/2021: J0224