Drug Coverage Policy

Effective Date **5/1/2024**
Coverage Policy Number **IP0095**

Metabolic Disorders – Primary Hyperoxaluria – Oxlumo

- Oxlumo™ (lumasiran subcutaneous injection – Alnylam)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Medical Necessity Criteria

Oxlumo is considered medically necessary when the following criteria are met:

1. **Primary Hyperoxaluria Type 1**. Individual meets **ALL** of the following criteria:
    A. Diagnosis of primary hyperoxaluria is confirmed by **ONE** of the following:
        i. A genetic test confirming biallellic pathogenic variants in the *AGXT* gene
        ii. Liver biopsy demonstrating absent, or significantly reduced AGT activity

B. Documentation of **ONE** of the following:
    i. Urinary oxalate excretion ≥ 0.7 mmol/24 hours/1.73 meter^2
    ii. Urinary oxalate/creatinine ratio above the laboratory's age-specific normal reference range
    iii. Plasma oxalate level ≥ 20 µmol/L
C. Medication is prescribed by or in consultation with a nephrologist, urologist, or medical geneticist

Dosing. For loading dose, up to 6 mg/kg administered subcutaneously once a month for three doses

1. For maintenance dosing, **ONE** of the following:
    A. 3 mg/kg administered subcutaneously once every month (body weight less than 10 kg)
    B. 3 mg/kg administered subcutaneously once every 3 months (body weight 20 kg and above)
    C. 6 mg/kg administered subcutaneously once every 3 months (body weight 10 kg to less than 20 kg)

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Reauthorization Criteria

Continuation of lumasiran (Oxlumo) is considered medically necessary for Primary Hyperoxaluria Type 1 when initial criteria are met AND beneficial response is demonstrated by **ONE** of the following:

1. Reduction in urinary oxalate excretion from baseline
2. Reduction in urinary oxalate/creatinine ratio from baseline
3. Reduction in plasma oxalate levels from baseline
4. Improved, or stabilized clinical signs/symptoms of primary hyperoxaluria type 1 (for example, nephrocalcinosis, formation of renal stones, renal impairment)

Authorization Duration

Initial approval duration: 6 months.
Reauthorization approval duration: 12 months.

Conditions Not Covered

Any other use is considered experimental, investigational or unproven, including the following (this list may not be all inclusive):

1. **Primary Hyperoxaluria Type 2 (PH2).**
    Oxlumo is not expected to be effective for the treatment of PH2 because its mechanism of action does not affect the metabolic pathways causing hypoxaluria in PH2.[1] Oxlumo has not been studied for the treatment of individuals with PH2.

2. **Primary Hyperoxaluria Type 3 (PH3).**

Oxlumo is not expected to be effective for the treatment of PH3 because its mechanism of action does not affect the metabolic pathways causing hypoxaluria in PH3.[1] Oxlumo has not been studied for the treatment of individuals with PH3.

3. **Status-Post Liver Transplant.**
   Individuals were excluded from clinical trials with a history of liver transplant.[2, 3] Liver transplant is potentially curative as it corrects the underlying enzymatic defect due to mutations of the AGXT gene.

4. **Concurrent use of Oxlumo with Rivfloza (nedosiran subcutaneous injection).** Rivfloza is another small interfering RNA agent and should not be used with Oxlumo.

Coding Information

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J0224	Injection, lumasiran, 0.5 mg

Background

OVERVIEW
Primary hyperoxaluria type 1 is a rare autosomal recessive inborn error of glyoxylate metabolism that results in the overproduction of oxalate, which forms insoluble calcium oxalate crystals that accumulate in the kidney and other organs, leading to issues such as nephrocalcinosis, formation of renal stones, and renal impairment.[2] Mutations in the alanine:glyoxylate aminotransferase gene (AGXT) cause primary hyperoxaluria type 1.[3] Liver transplantation is the only curative intervention for primary hyperoxaluria type 1 as it corrects the underlying enzymatic defect due to mutations of the AGXT gene.[2-4]

Clinical Efficacy
The efficacy of Oxlumo for the treatment of primary hyperoxaluria type 1 has been evaluated in three pivotal studies.[1,5,6,7] One study included patients ≥ 6 years of age with confirmed AGXT mutations and urinary oxalate excretion ≥ 0.7 mmol/24 hr/1.73 m^2.[5] A second, single-arm study included patients < 6 years of age with a genetically-confirmed primary hyperoxaluria type 1 diagnosis and an elevated spot urinary oxalate:creatinine ratio for age/weight.[6] Efficacy in regard to the urinary oxalate:creatinine ratio was evaluated at Month 6. A third clinical trial evaluated patients of any age with genetically-confirmed primary hyperoxaluria type 1 and a plasma oxalate level ≥ 20 µmol/L.[7] The primary efficacy endpoint of the mean reduction in plasma oxalate was assessed following 6 months of Oxlumo therapy.

Dosing
Dosing of Oxlumo is weight-based and consists of loading doses followed by maintenance dosing that begins 1 month after the last loading dose.[1] If the patient is receiving hemodialysis, administer Oxlumo after hemodialysis if administered on dialysis days.

Table 1. Oxlumo Weight-Based Dosing Regimen.[1]

Body Weight	Loading Dose	Maintenance 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)

* Begin 1 month after the last loading dose.

References

1. Oxlumo™ subcutaneous injection [prescribing information]. Cambridge, MA: Alnylam; October 2022.
2. Milliner DS, Harris PC, Cogal AG, et al. Primary Hyperoxaluria Type 1. Gene Reviews® Available at: https://www.ncbi.nlm.nih.gov/books/NBK1283/. Updated February 10, 2022. Accessed on September 14, 2023.
3. Primary Hyperoxaluria: MedlinePlus Genetics. U.S. National Library of Medicine; National Institutes of Health; Department of Health and Human Services. Available at: https://medlineplus.gov/genetics/condition/primary-hyperoxaluria/#resources. Updated November 8, 2021. Accessed on September 14, 2023.
4. Cochat P, Rumsby G. Primary hyperoxaluria. *N Engl J Med*. 2013;369(7):649-658.
5. Garrelfs SF, Frishberg Y, Hulton SA, et al. Lumasiran, an RNAi therapeutic for primary hyperoxaluria Type 1. *N Engl J Med*. 2021;384(13):1216-1226.
6. Sas DJ, Magen D, Hayes W, et al. Phase 3 trial of lumasiran for primary hyperoxaluria type 1: a new RNAi therapeutic in infants and young children. *Genet Med*. 2022;24(3):654-662.
7. Michael M, Groothoff JW, Shasha-Lavsky H, et al. Lumasiran for advanced primary hyperoxaluria type 1: phase 3 ILLUMINATE-C. *Am J Kidney Dis*. 2022 July 14. [Epub ahead of print].

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	It was added under Conditions not recommended for approval that concurrent use of Oxlumo and Rivfloza should not be used. Policy name changed to Metabolic Disorders – Primary Hyperoxaluria – Oxlumo Utilization Management Medical Policy.	5/1/2024
Selected Revision	**Updated coding:** **Added** J0224	09/10/2024

The policy effective date is in force until updated or retired.