Drug Coverage Policy

Effective Date 03/01/2025
Coverage Policy Number.....IP0095
Policy Title..... Primary Hyperoxaluria – Oxlumo

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.

Cigna Healthcare Coverage Policy

OVERVIEW
Oxlumo, a hydroxyacid oxidase 1 (*HAO1*)-directed small interfering RNA, is indicated for the treatment of **primary hyperoxaluria type 1** to lower urinary and plasma oxalate levels in pediatric and adult patients.[1]

Disease 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.

Medical Necessity Criteria

Documentation: Documentation is required for use of Oxlumo as noted in the criteria. Documentation may include, but is not limited to chart notes, laboratory tests, claims records, and/or other information. Subsequent coverage reviews for a patient who has previously met the documentation requirements and related criteria in the *Primary Hyperoxaluria – Oxlumo* policy through the Coverage Review Department, and who is requesting reauthorization, are NOT required to resubmit documentation for reauthorization, except for the criterion requiring documentation of a continued benefit from Oxlumo therapy.

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

FDA-Approved Indication

1. **Primary Hyperoxaluria Type 1**. Approve Oxlumo for the duration noted if the patient meets ONE of the following (A or B):
   A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, and iv):

i. Documentation provided that the patient has had a genetic test confirming the diagnosis of Primary Hyperoxaluria Type 1 via identification of biallelic pathogenic variants in the alanine:glyoxylate aminotransferase gene (AGXT); AND

ii. Patient meets ONE of the following (a, b, or c):

a) Documentation provided that the patient has a urinary oxalate excretion ≥ 0.5 mmol/24 hours/1.73 meters^2 with the absence of secondary sources of oxalate; OR

b) Documentation provided that the patient has a urinary oxalate:creatinine ratio above the age-specific upper limit of normal; OR

c) Documentation provided that the patient has a plasma oxalate level ≥ 20 µmol/L; AND

iii. Patient has not previously received a liver transplant for Primary Hyperoxaluria Type 1; AND

iv. The medication is prescribed by or in consultation with a nephrologist or urologist.

B) Patient is Currently Receiving Oxlumo. Approve for 1 year if the patients meets BOTH of the following (i and ii):

i. Documentation provided that the patient is continuing to derive benefit from Oxlumo, according to the prescriber; AND
Note: Examples of responses to Oxlumo therapy are reduced urinary oxalate excretion, decreased urinary oxalate:creatinine ratio, or reduced plasma oxalate levels from baseline (i.e., prior to Oxlumo therapy) or improved or stabilized clinical signs/symptoms of Primary Hyperoxaluria Type 1 (e.g., nephrocalcinosis, formation of renal stones, renal impairment).

ii. Patient has not previously received a liver transplant for Primary Hyperoxaluria Type 1.

Dosing. Approve the following dosing regimens.

A) Initially, approve up to 6 mg/kg administered subcutaneously not more frequently than once every month for three doses; AND/OR

B) For maintenance dosing, approve ONE of the following (i or ii):

i. 3 mg/kg administered subcutaneously not more frequently than once every month; OR

ii. 6 mg/kg administered subcutaneously not more frequently than once every 3 months.

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.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

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. **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

References

1. Oxlumo™ subcutaneous injection [prescribing information]. Cambridge, MA: Alnylam; September 2023.
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 August 15, 2024. Accessed on November 15, 2024.
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. Accessed on November 15, 2024.
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].
8. Michael M, Harvey E, Milliner DS, et al. Diagnosis and management of primary hyperoxalurias: best practices. *Pediatr Nephrol*. 2024;39(11):3143-3155.

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:**	09/10/2024

	Added J0224	
Annual Revision	No criteria changes	2/15/2025
Selected Revision	Added and defined documentation requirements to the policy. **Primary Hyperoxaluria Type 1:** For Initial Therapy, removed "Liver biopsy demonstrating absent, or significantly reduced AGT Activity" as a means of confirming diagnosis. The option of approval that the patient has a urinary oxalate excretion ≥ 0.7 mmol/24 hours/1.73 m^2 was updated to the patient has a urinary oxalate excretion ≥ 0.5 mmol/24 hours/1.73 m^2 with the absence of secondary sources of oxalate. Added the requirement that the patient has not previously received a liver transplant (previously, was in the "Conditions Not Covered" section as "Status Post Liver Transplant"). Removed "medical geneticist" from the list of specialist prescribers. For Patient is Currently Receiving Oxlumo, added the requirement that the patient has not previously received a liver transplant (previously, was in the "Conditions Not Covered" section as "Status Post Liver Transplant"). Relocated the examples of beneficial response to a "Note".	03/01/2025

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