VENTURA COUNTY
HEALTH CARE PLAN

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Metabolic Disorders – Primary Hyperoxaluria – Oxlumo Utilization Management Medical Policy

- Oxlumo™ (lumasiran subcutaneous injection – Alnylam)

REVIEW DATE: 11/20/2024; selected revision 12/18/2024, 02/05/2025

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.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Oxlumo. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Oxlumo as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Oxlumo to be prescribed by or in consultation with a physician who specializes in the condition being treated. All reviews will be forwarded to the Medical Director for evaluation.

Documentation: Documentation is required for use of Oxlumo as noted in the criteria as **[documentation required]**. 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 *Oxlumo Utilization Management Medical 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Oxlumo is recommended in those who meet the following criteria:

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.** 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*) **[documentation required]**; AND
     - **ii.** Patient meets ONE of the following (a, b, or c):
       - **a)** Patient has a urinary oxalate excretion ≥ 0.5 mmol/24 hours/1.73 meters^2 with the absence of secondary sources of oxalate **[documentation required]**; OR
       - **b)** Patient has a urinary oxalate:creatinine ratio above the age-specific upper limit of normal **[documentation required]**; OR
       - **c)** Patient has a plasma oxalate level ≥ 20 µmol/L **[documentation required]**; 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; OR
   - **B)** Patient is Currently Receiving Oxlumo. Approve for 1 year if the patients meets BOTH of the following (i and ii):
     - **i.** The patient is continuing to derive benefit from Oxlumo, according to the prescriber **[documentation required]**.

       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.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Oxlumo is not recommended in the following situations:

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 hyperoxaluria in PH2.[1] Oxlumo has not been studied for the treatment of patients 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 hyperoxaluria in PH3.[1] Oxlumo has not been studied for the treatment of patients 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.

4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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.

HISTORY

Type of Revision	Summary of Changes	Review 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 from Metabolic Disorders – Oxlumo Utilization Management Medical Policy to Metabolic Disorders – Primary Hyperoxaluria – Oxlumo Utilization Management Medical Policy.	11/01/2023
Annual Revision	No criteria changes.	11/20/2024
Selected Revision	**Primary Hyperoxaluria Type 1:** For Initial Therapy, the option of approval that the patient has a urinary oxalate excretion ≥ 0.7 mmol/24 hours/1.73 m2 was revised to the patient has a urinary oxalate excretion ≥ 0.5 mmol/24 hours/1.73 m2 with the absence of secondary sources of oxalate. For Patient is Currently Receiving Oxlumo, the requirement that the patient is continuing to derive benefit from Oxlumo was revised to remove the qualifier that this was "as determined by the most recent (i.e., within the past 6 months) objective measurement". Also, the requirement that the patient has not previously received a liver transplant was added to the Patient is Currently Receiving Oxlumo criteria set (previously, was only in the Initial Therapy criteria set).	12/18/2024
Selected Revision	**Primary Hyperoxaluria Type 1:** For diagnosis confirmed by genetic testing, rephrased the term "mutation" to "biallelic pathogenic variants".	02/05/2025