PRIOR AUTHORIZATION POLICY

POLICY: Metabolic Disorders – Primary Hyperoxaluria – Oxlumo Prior Authorization Policy
- Oxlumo™ (lumasiran subcutaneous injection – Alnylam)

REVIEW DATE: 11/20/2024

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.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Oxlumo. 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 Prior Authorization 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 an alanine:glyoxylate aminotransferase gene (AGXT) mutation **[documentation required]**; AND
     - **ii.** Patient meets ONE of the following (a, b, or c):
       - **a)** Patient has a urinary oxalate excretion ≥ 0.7 mmol/24 hours/1.73 m^2 **[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.
   - **B)** Patient is Currently Receiving Oxlumo. Approve for 1 year if, according to the prescriber, the patient is continuing to derive benefit from Oxlumo as determined by the most recent (i.e., within the past 6 months) objective measurement **[documentation required]**.
     Note: Examples of objective measurements of a response 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).

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; October 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].