BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

EVIDENCE-BASED CRITERIA	**ORIGINAL EFFECTIVE DATE: 01/15/24**
SECTION: SPECIALTY MEDICAL DRUGS	**LAST REVIEW DATE: 11/16/23**
	CURRENT EFFECTIVE DATE: 02/15/24
	LAST CRITERIA REVISION DATE: 02/15/24
NEXT ANNUAL REVIEW DATE: 4TH QTR 2024	**ARCHIVE DATE:**

OXLUMO® (lumasiran)

Non-Discrimination Statement is located at the end of this document.

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Evidence-Based Criteria must be read in its entirety to determine coverage eligibility, if any.

This Evidence-Based Criteria provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Evidence-Based Criteria are subject to change as new information becomes available.

For purposes of this Evidence-Based Criteria, the terms "experimental" and "investigational" are considered to be interchangeable.

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OXLUMO® (lumasiran)

Criteria:

Refer to FDA website for current indications and dosage.

- **Criteria for initial therapy:** Oxlumo (lumasiran) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Nephrologist or Urologist

  2. Individual has a confirmed diagnosis of primary hyperoxaluria type 1 (PH1) as indicated by **ALL** of the following:

     - Documentation of biallelic pathogenic variants in alanine:glyoxylate aminotransferase (AGT or AGXT) gene **OR** liver biopsy demonstrating AGT deficiency
     - Documentation of elevated oxalate indicated by **ONE** of the following:

       a. Urinary oxalate excretion ≥ 0.7 mmol/24 hours/1.73 meter^2
       b. Urinary oxalate/creatinine ratio above the laboratory's age-specific normal reference range
       c. Plasma oxalate level ≥ 20 µmol/L or >1.76mg/L

  3. Individual does **NOT** have **ANY** of the following:

     - Previous or planned liver transplant
     - Secondary causes of hyperoxaluria (e.g., diet with excessive intake of oxalate, gastric bypass surgery, inflammatory bowel disease (IBD), or other intestinal disorders)

  4. The Attestation for Oxlumo Treatment form (see below) has been signed by the physician (or designee)

  Initial approval duration: 6 months

  Approval conditions:
  If an individual meets all coverage guideline criteria and is approved to receive treatment, the requesting provider attests and agrees to submit clinical outcomes data and information.

  Required Outcomes Measurements: Provider submits **documentation** of medication administration, missed doses, and/or discontinuation of the medication.

- **Criteria for continuation of coverage (renewal request):** Oxlumo (lumasiran) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

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1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Nephrologist or Urologist

2. Individual has a confirmed diagnosis of primary hyperoxaluria type 1 (PH1) as indicated by documentation of biallelic pathogenic variants in alanine: glyoxylate aminotransferase (AGT or AGXT) gene **OR** liver biopsy demonstrating AGT deficiency

3. Individual's condition has responded while on therapy with response defined as **BOTH** of the following:

   - Reduction in urinary oxalate excretion, urinary oxalate:creatinine ratio, or plasma oxalate levels from baseline
   - Improvement, stabilization or slowed worsening of clinical signs and symptoms of Primary Hyperoxaluria Type 1 (e.g., nephrocalcinosis, formation of renal stones, renal impairment)

4. Individual has been adherent with the medication

5. Individual has does not have a previous or planned liver transplant

6. The Attestation for Oxlumo Treatment form (see below) has been signed by the physician (or designee) [Note: Signed treatment form only needed once for any treating physician and may not be needed on renewal.]

Renewal duration: 12 months

Approval conditions:
If an individual meets all coverage guideline criteria and is approved to receive treatment, the requesting provider attests and agrees to submit clinical outcomes data and information.

Required Outcomes Measurements: Provider submits **documentation** of medication administration, missed doses, and/or discontinuation of the medication.

- Oxlumo (lumasiran) for all other indications not previously listed is considered ***experimental or investigational*** when any **ONE** or more of the following criteria are met:

1. Lack of final approval from the appropriate governmental regulatory bodies (e.g., Food and Drug Administration); or
2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes; or
3. Insufficient evidence to support improvement of the net health outcome; or
4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; or
5. Insufficient evidence to support improvement outside the investigational setting.

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OXLUMO® (lumasiran)

These indications include, *but are not limited to:*

- Treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, or duration.

Attestations for Oxlumo Treatment

Physician Name: _____

Individual Name: _____ DOB**:** _____

- The Physician is responsible for filling out this form.
- All elements must be initialed, and the form must be signed by the Physician (or designee)
- Incomplete forms will be returned to acquire missing information, initial, signature, or date.
- Return completed form to BCBSAZ.

Physician Agreement:

- Physician to initial by each element and date and sign to show willingness to participate.
- Documentation may include, but is not limited to, chart notes, laboratory test results, claims records, and/or other information.

Initials:

_____ I verify that the patient will be closely followed and monitored for progression of disease

_____ I agree to submit clinical outcomes data and information

_____ I agree to submit lab Oxlumo administration records including dates administered and dose administered

_____ I agree to submit documentation if the individual misses a dose OR discontinues the medication

Provider (or designee) Signature: _____

Date: _____

Description:

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

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OXLUMO® (lumasiran)

Primary hyperoxaluria is a rare disorder of glyoxylate metabolism characterized by the overproduction of oxalate, which is poorly soluble and deposited as calcium oxalate in the kidneys and urinary tract, leading to the formation of painful and recurrent nephrolithiasis (renal stones), nephrocalcinosis, and renal failure. Compromised renal function exacerbates the disease as the excess oxalate can no longer be effectively excreted, resulting in subsequent accumulation and crystallization in bones, eyes, skin, and heart, leading to severe illness and death.

Liver transplantation is the only curative intervention as it corrects the underlying enzymatic defect due to mutations of the AGXT gene. In patients with significant chronic renal disease, renal transplant may also be required. Lumasiran is the first specific treatment for PH1. Lumasiran is a subcutaneously administered RNA interference (RNAi) therapeutic that silences the HAO1 gene, which encodes for a glycolate oxidase enzyme. By silencing the HAO1 gene, levels of glycolate oxidase are depleted, decreasing production of oxalate, the metabolite that directly contributes to the pathophysiology of primary hyperoxaluria type 1.

Definitions:

Oxlumo Weight-Based Dosing Regimen

Body Weight	Loading Dose	Maintenance Dose*
Less than 10 kg	6 mg/kg once monthly x 3 doses	3mg/kg once monthly
10 kg to less than 20 kg	6 mg/kg once monthly x 3 doses	6mg/kg once every 3 months (quarterly)
20kg and greater	3 mg/kg once monthly x 3 doses	3mg/kg once every 3 months (quarterly)

*Beginning month after the last loading dose

History:	Date:	Activity:
Pharmacy and Therapeutics Committee	02/15/24	Revisions of guideline
Pharmacy and Therapeutics Committee	11/16/23	Approved guideline
Clinical Pharmacist	10/24/23	Development

Coding:

HCPCS: J0224

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Resources:

Literature reviewed 11/16/23. We do not include marketing materials, poster boards and non-published literature in our review.

1. Garrelfs SF, Frishberg Y, Hulton SA, et al; ILLUMINATE-A Collaborators. Lumasiran, an RNAi therapeutic for primary hyperoxaluria type 1. *N Engl J Med*. 2021;384(13):1216-1226.

2. Michael M, Groothoff JW, Shasha-Lavsky H, et al. Lumasiran for advanced primary hyperoxaluria type 1: Phase 3 ILLUMINATE-C Trial. *Am J Kidney Dis*. 2022;81(2):145-155.

3. Niaudet P. Primary hyperoxaluria. In: UpToDate, Matoo TK, Hoppin AG. (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last update on August 16, 2023. Accessed October 13, 2023.

4. Oxlumo (lumasiran) prescribing information, revised by Alnylam Pharmaceuticals, Inc. 10/2022. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 13, 2023.

5. 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.

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Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability or sex, you can file a grievance with: BCBSAZ's Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, crc@azblue.com. You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ's Civil Rights Coordinator is available to help you. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at: U.S. Department of Health and Human Services, 200 Independence Avenue SW., Room 509F, HHH Building, Washington, DC 20201, 1–800–368–1019, 800–537–7697 (TDD). Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html