PROVIDER POLICIES & PROCEDURES

OXLUMO® (LUMASIRAN)

The primary purpose of this document is to assist providers enrolled in the Connecticut Medical Assistance Program (CMAP) with the information needed to support a medical necessity determination for OXLUMO (lumasiran). By clarifying the information needed for prior authorization of services, HUSKY Health hopes to facilitate timely review of requests so that individuals obtain the medically necessary care they need as quickly as possible.

OXLUMO 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.

Primary hyperoxalurias (PHs) are rare inborn errors of glyoxylate metabolism characterized by the overproduction of oxalate, which is deposited as calcium oxalate in various organs. Primary hyperoxalurias are caused by mutations in one of the three genes that encode enzymes involved in glyoxylate metabolism. As oxalate is primarily excreted in the urine, the kidney is the prime target for oxalate deposition, which leads to end-stage kidney disease in many cases.

PH type 1 is due to the defects in the gene that encodes the hepatic peroxisomal enzyme alanine: glyoxylate aminotransferase (AGT), a pyridoxal 5'-phosphate-dependent enzyme, which is involved in the transamination of glyoxylate to glycine. Although PH type 1 is the more common of the three types of PH, accounting for approximately 80 percent of patients with PH, it is a rare disorder with a prevalence of one to three per million in Europe and North America.

CLINICAL GUIDELINE

Coverage guidelines for the use of OXLUMO will be made in accordance with the DSS definition of Medical Necessity. The following criteria are guidelines *only*. Coverage guidelines are based on an assessment of the individual and their unique clinical needs. If the guidelines conflict with the definition of Medical Necessity, the definition of Medical Necessity shall prevail. The guidelines are as follows:

Initial Authorization:

OXLUMO may be considered medically necessary if the following criteria are met:

A. The individual has a diagnosis of primary hyperoxaluria type 1 (PH1) confirmed by one of the following:
    1. Genetic testing confirming presence of a mutation in the alanine:glyoxylate aminotransferase (AGXT) gene; or
    2. Liver biopsy confirming AGT enzyme deficiency; **AND**
B. The individual has one of the following clinical signs or symptoms of PH1:
    a. Elevated urine oxalate excretion (body surface area-normalized daily urine oxalate excretion output ≥ 0.7 mmol/1.73 m^2); **OR**

b. Elevated plasma oxalate concentration > 20 µmol/L or > 1.76 mg/L; **OR**
c. Urine oxalate excretion : creatinine ratio above age-specific upper limit of normal; **AND**

C. The medication is prescribed by, or in consultation with a nephrologist, urologist, or an expert in the treatment of primary hyperoxaluria type 1; **AND**
D. The medication will not be used in combination with nedosiran (RIVFLOZA®); **AND**
E. The individual has not had a liver transplant; **AND**
F. The physician will follow all FDA recommendations for dosing and administration.

Continuation of Therapy

A. The individual is currently receiving treatment with Oxulmo; **AND**
B. The individual's urinary oxalate excretion level, plasma oxalate level or urine oxalate excretion: creatinine ratio has decreased or normalized since initiation of therapy; **AND**
C. The individual is not taking nedosiran; **AND**
D. The physician will continue to follow all FDA recommendations for dosing and administration.

Investigational and Not Medically Necessary

Use of OXLUMO as treatment for primary hyperoxaluria type 2 and type 3 is considered investigational and not medically necessary.

Use of OXLUMO for any other indications is considered investigational and not medically necessary.

NOTE: EPSDT Special Provision

Early and Periodic Screening, Diagnosis, and Treatment (EPSDT) is a federal Medicaid requirement that requires the Connecticut Medical Assistance Program (CMAP) to cover services, products, or procedures for Medicaid enrollees under 21 years of age where the service or good is medically necessary health care to correct or ameliorate a defect, physical or mental illness, or a condition identified through a screening examination. The applicable definition of medical necessity is set forth in Conn. Gen. Stat. Section 17b-259b (2011) [ref. CMAP Provider Bulletin PB 2011-36].

PROCEDURE

Prior authorization of OXLUMO is required. Coverage determinations will be based upon a review of requested and/or submitted case-specific information.

The following information is needed to review requests for OXLUMO**:**

- Fully completed State of Connecticut, Department of Social Services HUSKY Health Outpatient Prior Authorization Form (to include physician's order and signature)
- Clinical information supporting medical necessity as outlined in the Clinical Guideline section of this policy including:
    1. Genetic testing results confirming mutation in the AGXT gene or liver biopsy results confirming AGT enzyme deficiency
    2. For Initial Requests ONLY:
        i. Baseline lab work showing elevation of at least ONE of the following:
            1. Urinary oxalate excretion level; **OR**
            2. Plasma oxalate level; **OR**
            3. Urine oxalate excretion : creatinine ratio
    3. For Continuation of therapy ONLY:

i. Repeat lab work showing a decrease from baseline of at least ONE of the following:
    1. Urinary oxalate excretion level; **OR**
    2. Plasma oxalate level; **OR**
    3. Urine oxalate excretion : creatinine ratio
- Other information as requested by CHNCT

Requesting Authorization
Requests must be submitted by the ordering physician and faxed to the number listed on the request form. Questions regarding this form should be directed to the HUSKY Health Program Utilization Management Department at 1.800.440.5071 (select option for medical authorizations).

Initial Authorization
Initial approval of OXLUMO will be for 6 months.

Re-authorization
Requests for continuation of OXLUMO will be reviewed at 12-month intervals.

EFFECTIVE DATE
This Policy for the prior authorization of OXLUMO, for individuals covered under the HUSKY Health Program is effective July 1, 2021.

LIMITATIONS
Not Applicable

CODES:

Code	Definition
J0224	Injection, lumasiran, 0.5 mg

DEFINITIONS
1. **HUSKY A**: Connecticut children and their parents or a relative caregiver; and pregnant women may qualify for HUSKY A (also known as Medicaid). Income limits apply.
2. **HUSKY B**: Uninsured children under the age of 19 in higher income households may be eligible for HUSKY B (also known as the Children's Health Insurance Program) depending on their family income level. Family cost-sharing may apply.
3. **HUSKY C**: Connecticut residents who are age 65 or older or residents who are ages 18-64 and who are blind, or have another disability, may qualify for Medicaid coverage under HUSKY C (this includes Medicaid for Employees with Disabilities (MED-Connect), if working). Income and asset limits apply.
4. **HUSKY D**: Connecticut residents who are ages 19-64 without dependent children and who: (1) do not qualify for HUSKY A; (2) do not receive Medicare; and (3) are not pregnant, may qualify for HUSKY D (also known as Medicaid for the Lowest-Income populations).
5. **HUSKY Health Program**: The HUSKY A, HUSKY B, HUSKY C, HUSKY D and HUSKY Limited Benefit programs, collectively.
6. **HUSKY Limited Benefit Program or HUSKY, LBP**: Connecticut's implementation of limited health insurance coverage under Medicaid for individuals with tuberculosis or for family planning purposes

and such coverage is substantially less than the full Medicaid coverage.

7. **Medically Necessary or Medical Necessity**: (as defined in Connecticut General Statutes § 17b-259b) Those health services required to prevent, identify, diagnose, treat, rehabilitate or ameliorate an individual's medical condition, including mental illness, or its effects, in order to attain or maintain the individual's achievable health and independent functioning provided such services are: (1) Consistent with generally-accepted standards of medical practice that are defined as standards that are based on (A) credible scientific evidence published in peer-reviewed medical literature that is generally recognized by the relevant medical community, (B) recommendations of a physician-specialty society, (C) the views of physicians practicing in relevant clinical areas, and (D) any other relevant factors; (2) clinically appropriate in terms of type, frequency, timing, site, extent and duration and considered effective for the individual's illness, injury or disease; (3) not primarily for the convenience of the individual, the individual's health care provider or other health care providers; (4) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the individual's illness, injury or disease; and (5) based on an assessment of the individual and his or her medical condition.
8. **Prior Authorization**: A process for approving covered services prior to the delivery of the service or initiation of the plan of care based on a determination by CHNCT as to whether the requested service is medically necessary.

ADDITIONAL RESOURCES AND REFERENCES:

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- Hulton SA, Groothoff JW, Frishberg Y, et al. Randomized Clinical Trial on the Long-Term Efficacy and Safety of Lumasiran in Patients With Primary Hyperoxaluria Type 1. Kidney Int Rep. 2021 Dec 11;7(3):494-506. doi: 10.1016/j.ekir.2021.12.001.
- ILLUMINATE-A: A Phase 3 Randomized, Double-Blind, Placebo-Controlled Study With an Extended Dosing Period to Evaluate the Efficacy and Safety of Lumasiran in Children and Adults With Primary Hyperoxaluria Type 1. Accessed on December 3, 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT03681184
- ILLUMINATE-B: An Open-Label Study to Evaluate the Efficacy, Safety, Pharmacokinetics, and Pharmacodynamics of Lumasiran in Infants and Young Children With Primary Hyperoxaluria Type 1. Accessed on December 3, 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT03905694
- Liebow A, Li X, Racie T, et al. An Investigational RNAi Therapeutic Targeting Glycolate Oxidase Reduces Oxalate Production in Models of Primary Hyperoxaluria. *J Am Soc Nephrol*. 2017;28(2):494-503. doi:10.1681/ASN.2016030338
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- OXLUMO [Prescribing Information]. Cambridge, MA: Alnylam Pharmaceuticals, Inc.; Revised September 2023
- 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. 2023 Feb;81(2):145-155.e1. doi: 10.1053/j.ajkd.2022.05.012.
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- U.S. Food and Drug Administration. FDA Approves First Drug to Treat Rare Metabolic Disorder.

November 23, 2020. Accessed on December 3, 2020. Available at: https://www.fda.gov/news-events/press-announcements/fda-approves-first-drug-treat-rare-metabolic-disorder
- Wood KD, Holmes RP, Knight J. RNA interference in the treatment of renal stone disease: Current status and future potentials. *Int J Surg*. 2016;36(Pt D):713-716. doi:10.1016/j.ijsu.2016.11.027

PUBLICATION HISTORY

Status	Date	Action Taken
Original publication	June 2021	Reviewed and approved at the January 13, 2021 CHNCT Medical Reviewer meeting. Reviewed and approved at the June 21, 2021 CHNCT Clinical Quality Subcommittee meeting. Approved by DSS on June 28, 2021.
Reviewed	June 2022	Reviewed and approved without changes at the April 27, 2022 CHNCT Medical Reviewer meeting. Reviewed and approved without changes by the CHNCT Clinical Quality Subcommittee on June 20, 2022. Approved by DSS on July 5, 2022.
Updated	June 2023	Updated criteria to indicate that Oxlumo may be prescribed by or in consultation with a medical geneticist, nephrologist, urologist, or an expert in the treatment of primary hyperoxaluria type 1d, endocrinologist removed. Removed specific eGFR requirement. Changed 24-hour urine to urine or plasma oxalate levels. Changed review time frame from 6 months to 12 months. Updated code. Changes reviewed and approved at the April 12, 2023, CHNCT Medical Reviewer meeting. Changes approved by the CHNCT Clinical Quality Subcommittee on June 19, 2023. Approved by DSS on June 28, 2023.
Updated	April 2024	Updated description of Oxulmo to match prescribing information with regards to lowering urinary “and plasma” oxalate levels. Several grammatical changes made. Added criteria in both initial authorization and reauthorization sections regarding the use of Oxulmo in combination with nedosiran. Added the following to information necessary for review: "genetic testing results confirming mutation in th AGXT gene or liver biopsy results confirming AGT enzyme deficiency" Updated references. Changes reviewed and approved at the April 10, 2024, CHNCT Medical Reviewer meeting. Changes approved by the CHNCT Clinical Quality Subcommittee on June 17, 2024. Approved by DSS on June 26, 2024.
Updated	April 2025	Updated to add requirement of clinical signs or symptoms of PH1 into initial authorization criteria. Removed medical geneticist as a provider type specified in part C of initial criteria. Updated to add liver transplant exclusion criteria requirement. Updated verbiage in part B of continuation of therapy criteria to include urine oxalate excretion: creatinine ratio component. Clarified lab work needed to review requests in the procedure section. Changes reviewed and approved at the April 9, 2025, CHNCT Medical Reviewer meeting. Changes approved by the CHNCT Clinical Quality Subcommittee on June 16, 2025. Approved by DSS on July 9, 2025.