Prior Authorization Review Panel

CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	**Submission Date: 02/01/2024**
Policy Number: PA.CP.PHAR.473	**Effective Date: 04/2021** **Revision Date: 01/2024**
Policy Name: Lumasiran (Oxlumo)	

Type of Submission – Check all that apply:

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL -** *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any changes or clarifying information for the policy below:

1Q 2024 annual review: for reauthorization added decrease from baseline in POx levels along with symptomatic improvement as a pathway for reauthorization; references reviewed and updated.

Name of Authorized Individual (Please type or print): **Venkateswara R. Davuluri, MD**	**Signature of Authorized Individual:**

Clinical Policy: Lumasiran (Oxlumo)

Reference Number: PA.CP.PHAR.473
Effective Date: 04/2021
Last Review Date: 01/2024

Coding Implications
Revision Log

Description
Lumasiran (Oxlumo™) is an RNAi therapeutic targeting glycolate oxidase (GO).

FDA Approved Indication(s)
Oxlumo is indicated for the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary and plasma oxalate levels in pediatric and adult patients.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Oxlumo is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Primary Hyperoxaluria Type 1 (must meet all)**:**

1. Diagnosis of PH type 1 confirmed by one of the following (a or b):
   a. Genetic testing confirming presence of mutations in the *AGXT* gene;
   b. Liver biopsy confirming AGT enzyme deficiency;
2. Prescribed by or in consultation with an endocrinologist, hepatologist, or nephrologist;
3. Documentation of one of the following (a, b or c):
   a. Urinary oxalate (UOx) excretion > 0.70 mmol/1.73 m^2/24 h, confirmed on repeat testing;
   b. Spot urinary oxalate-to-creatinine (UOx:Cr) molar ratio greater than normal for age *(see Appendix D for reference ranges)*, confirmed on repeat testing;
   c. Plasma oxalate (POx) levels ≥ 20 µmol/L;
4. Failure to achieve normalization of UOx excretion levels after at least three months of pyridoxine (vitamin B6) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   **Normal UOx excretion is <0.50 mmol (<45 mg)/1.73 m^2/day, or see Appendix D for reference ranges for age-specific spot UOx/Cr molar ratios.*
5. Member has not had a liver transplant;
6. If on dialysis, member is on hemodialysis only for at least 4 weeks;
7. Documentation of member's current body weight (in kg);
8. Dose does not exceed any of the following, based on body weight (a, b, or c):
   a. < 10 kg: 6 mg/kg per month for 3 doses followed by 3 mg/kg per month;
   b. 10 kg to < 20 kg: 6 mg/kg per month for 3 doses followed by 6 mg/kg every 3 months;
   c. ≥ 20 kg: 3 mg/kg per month for 3 doses followed by 3 mg/kg every 3 months.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Primary Hyperoxaluria Type 1 (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy as evidenced by one of the following (a or b):
   a. Decrease from baseline in UOx excretion of > 30%;
   b. Decrease from baseline in UOx excretion or plasma oxalate levels or improvement in spot UOx:Cr molar ratio, along with improvement in PH1 symptoms (e.g., nephrolithiasis, nephrocalcinosis, kidney function, ischemic skin ulcers, metabolic bone disease, refractory anemia, cardiomyopathy, abnormalities in cardiac conduction);
3. Member has not had a liver transplant;
4. Documentation of member's current body weight (in kg);
5. If request is for a dose increase, new dose does not exceed any of the following, based on body weight (a, b, or c):
   a. < 10 kg: 3 mg/kg per month;
   b. 10 kg to < 20 kg: 6 mg/kg every 3 months;
   c. ≥ 20 kg: 3 mg/kg every 3 months.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

eGFR: estimated glomerular filtration rate
FDA: Food and Drug Administration
GO: glycolate oxidase
PH1: primary hyperoxaluria type 1
POx: plasma oxalate
RNAi: RNA interference

UOx: urinary oxalate UOx:Cr: urinary oxalate-to-creatinine

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
pyridoxine	5-20 mg/kg PO QD	20 mg/kg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: Spot UOx/Cr Molar Ratio Reference Ranges in Spot Urine Samples

Age	Normal Values
0-6 months	< 325-360 mmol/mol (< 253-282 mg/g)
7-24 months	< 132-174 mmol/mol (< 103-136 mg/g)
2-5 years	< 98-101 mmol/mol (< 76-79 mg/g)
5-14 years	< 70-82 mmol/mol (< 55-64 mg/g)
> 16 years	< 40 mmol/mol (< 32 mg/g)

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
PH1	If weight is: • < 10 kg: 6 mg/kg/month SC for 3 doses followed by 3 mg/kg/month; • 10 kg to < 20 kg: 6 mg/kg/month SC for 3 doses followed by 6 mg/kg SC every 3 months; • ≥ 20 kg: 3 mg/kg/month SC for 3 doses followed by 3 mg/kg SC every 3 months	If weight is: • < 10 kg: 3 mg/kg/month; • 10 kg to < 20 kg: 6 mg/kg every 3 months; • ≥ 20 kg: 3 mg/kg every 3 months

VI. Product Availability
Solution in single-dose vial: 94.5 mg/0.5 mL

VII. References
1. Oxlumo Prescribing Information. Cambridge, MA: Alnylam Pharmaceuticals, Inc. September 2023. Available at www.Oxlumo.com. Accessed October 13, 2023.
2. Milliner DS, Harris PC, Cogal AG, et al. Primary hyperoxaluria type 1. 2002 Jun 19 [Updated 2017 Nov 30]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2020. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1283/pdf/Bookshelf_NBK1283.pdf. Accessed November 14, 2023.

3. 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 Jul 14:S0272-6386(22)00771-5.
4. Groothoff JW, Metry E, Deesker L, et al. Clinical practice recommendations for primary hyperoxaluria: an expert consensus statement from ERKNet and OxalEurope. Nature Reviews Nephrology. 2023;19:194-211.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J0224	Injection, lumasiran, 0.5 mg

Reviews, Revisions, and Approvals	Date
Policy created	04/2021
1Q 2022 annual review: references reviewed and updated.	01/2022
1Q 2023 annual review: HCPCS code updated; added new indication of lowering of plasma oxlate levels in PH1; removal of eGFR requirement, added ability to use plasma oxalate (POx) levels ≥ 20 µmol/L as documentation, and if on dialysis member is on hemodialysis only for at least 4 weeks based on study population characteristics in ILLUMINATE-C trial; references reviewed and updated.	01/2023
1Q 2024 annual review: for reauthorization added decrease from baseline in POx levels along with symptomatic improvement as a pathway for reauthorization; references reviewed and updated.	01/2024