Clinical Policy: Lumasiran (Oxlumo)

Reference Number: CP.PHAR.473
Effective Date: 11.23.20
Last Review Date: 02.25
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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 health plans affiliated with Centene Corporation® 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, nephrologist, urologist or medical geneticist;
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 has been on a stable hemodialysis regimen for at least 4 weeks and is not on peritoneal dialysis;
7. Oxlumo is not prescribed concurrently with Rivfloza®;
8. Documentation of member's current body weight (in kg);

9. 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:
Medicaid/HIM – 6 months
Commercial – 6 months or to the member's renewal date, whichever is longer

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
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. Improvement in PH1 symptoms (e.g., nephrolithiasis, nephrocalcinosis, kidney function, ischemic skin ulcers, metabolic bone disease, refractory anemia, cardiomyopathy, abnormalities in cardiac conduction) and one of the following (i, ii, or iii):
      i. Decrease from baseline in UOx excretion;
      ii. Decrease from baseline in plasma oxalate levels;
      iii. Improvement in spot UOx:Cr molar ratio;
3. Member has not had a liver transplant;

4. Oxlumo is not prescribed concurrently with Rivfloza;
5. Documentation of member's current body weight (in kg);
6. 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:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and 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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

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 SC; • 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 31, 2024.
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, 2024.

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	P&T Approval Date
Drug is now FDA approved – criteria updated per FDA labeling: added hepatologist and nephrologist specialists; added spot UOx/Cr molar ratio as an additional option for biochemical confirmation of PH1 diagnosis; added requirement for no prior liver transplant; added requirement for documentation of current weight in kg; added ability to reauthorize based on improvements in symptoms; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	01.05.21	02.21
Revised requirement for a minimum response to pyridoxine treatment from "> 30% reduction in UOx excretion" to "normalization of UOx excretion levels"; for reauthorization added improvement in spot UOx:Cr molar ratio along with symptomatic improvement as a pathway for reauthorization; references reviewed and updated.	06.06.21	08.21
1Q 2022 annual review: no significant changes; references reviewed and updated.	11.19.21	02.22
Template changes applied to other diagnoses/indications and continued therapy section.	09.28.22	
1Q 2023 annual review: HCPCS code updated; no sigifncant changes; references reviewed and updated. RT4: 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.	11.15.22	02.23
1Q 2024 annual review: for Commercial line of business changed approval duration to "6 months or duration of request, whichever is	10.13.23	02.24

Reviews, Revisions, and Approvals	Date	P&T Approval Date
less;", for reauthorization added decrease from baseline in POx levels along with symptomatic improvement as a pathway for reauthorization; references reviewed and updated.		
2Q 2024 annual review: added exclusion for concomitant use of Oxlumo with Rivfloza; clarified the intent of the dialysis criteria to reflect that the member should not be on peritoneal dialysis and if they are on hemodialysis then they have been on a stable hemodialysis regimen for at least 4 weeks, per the ILLUMINATE-C trial inclusion criteria; added urologists to the list of specialist prescribers; updated Commercial authorization duration language to match current standard language; references reviewed and updated.	02.29.24	05.24
1Q 2025 annual review: for initial criteria, added medical geneticist; references reviewed and updated.	10.31.24	02.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.