

Clinical Policy: Lumasiran (Oxlumo)

Reference Number: PA.CP.PHAR.473

Effective Date: 04/2021

Last Review Date: 04/2024

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 $> 0.70 \text{ mmol}/1.73 \text{ m}^2/24 \text{ h}$, 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 $\geq 20 \text{ } \mu\text{mol/L}$;
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 $< 0.50 \text{ mmol} (< 45 \text{ mg})/1.73 \text{ m}^2/\text{day}$, 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. $< 10 \text{ kg}$: 6 mg/kg per month for 3 doses followed by 3 mg/kg per month;
 - b. 10 kg to $< 20 \text{ kg}$: 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. 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. Oxlumio 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: 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 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	<p>If weight is:</p> <ul style="list-style-type: none"> < 10 kg: 6 mg/kg/month for 3 doses followed by 3 mg/kg/month; 10 kg to < 20 kg: 6 mg/kg/month for 3 doses followed by 6 mg/kg every 3 months; ≥ 20 kg: 3 mg/kg/month for 3 doses followed by 3 mg/kg every 3 months 	<p>If weight is:</p> <ul style="list-style-type: none"> < 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

- Oxlumo Prescribing Information. Cambridge, MA: Alnylam Pharmaceuticals, Inc. September 2023. Available at www.Oxlumo.com. Accessed February 29, 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 11, 2022.
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 oxalate levels in PH1; removal of eGFR requirement, added ability to use plasma oxalate (POx) levels $\geq 20 \mu\text{mol/L}$ 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
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; references reviewed and updated.	04/2024