Clinical Policy: Lumasiran (Oxlumo)

Reference Number: ERX.SPA.381
Effective Date: 11.23.20
Last Review Date: 08.21
Line of Business: Commercial, Medicaid

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 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 or b):
   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;
4. Documentation of estimated glomerular filtration rate (eGFR) > 30 mL/min/1.73 m^2;
5. 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.*
6. Member has not had a liver transplant;
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 ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by one of the following (a or b):
   a. Decrease from baseline in urinary oxalate excretion of > 30%;
   b. Decrease from baseline in UOx excretion 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 a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 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
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	If weight is: • < 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	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.; November 2020. Available at www.Oxlumo.com. Accessed June 6, 2021.
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 December 9, 2020.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	03.03.20	05.20
Drug is now FDA approved – criteria updated per FDA labeling: added hepatologist and nephrologist specialist; added spot UOx/Cr molar ratio as an additional option for biochemical confirmation of PH1 diagnosis; added requirement for no prior liver transplant; added ability to reauthorize based on improvements in symptoms; 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

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

be bound by the foregoing terms and conditions, in addition to the Site Use Agreement for Health Plans associated with Envolve Pharmacy Solutions.