



Louisiana

lumasiran (Oxlumo™)

Policy # 00746

Original Effective Date: 05/10/2021

Current Effective Date: 05/08/2023

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider lumasiran (Oxlumo™)[‡] for the treatment of primary hyperoxaluria type 1 (PH1) to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility for lumasiran (Oxlumo) will be considered when the following criteria are met:

- Initial therapy:
 - Patient has a diagnosis of PH1 confirmed by BOTH of the following:
 - ONE of the following:
 - ❖ Genetic confirmation of AGXT gene mutation; OR
 - ❖ Liver biopsy demonstrating absent or significantly reduced alanine:glyoxylate aminotransferase (AGT) activity; AND
 - ONE of the following:
 - ❖ Elevated urine oxalate (UOx) excretion as measured by body surface area-normalized daily UOx output greater than the upper limit of normal; OR
 - ❖ Elevated UOx excretion as measured by UOx:Creatinine ratio above age-specific upper limit of normal; OR
 - ❖ Elevated plasma oxalate (POx) concentration greater than the upper limit of normal; AND
 - Patient does not have secondary causes of hyperoxaluria (e.g., diet with excessive intake of oxalate, gastric bypass surgery, intestinal disorders, etc.); AND

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*(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

- Patient's estimated glomerular filtration rate (eGFR) is ≥ 30 mL/min/1.73 m²; AND
- Patient has NOT had a liver transplant; AND

*(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

- Dose will not exceed the FDA-labeled dose as described below:

Body weight	Loading dose	Maintenance Dose (begin 1 month after last loading dose)
Less than 10 kg	6 mg/kg once monthly for 3 doses	3 mg/kg once monthly
10 kg to less than 20 kg	6 mg/kg once monthly for 3 doses	6 mg/kg once every 3 months
20 kg and above	3 mg/kg once monthly for 3 doses	3 mg/kg once every 3 months

- Continuation therapy:

- Patient has received an initial authorization for Oxlumo; AND
- Liver transplantation has not occurred since previous authorization; AND
- (Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient has responded to therapy as demonstrated by a reduction of urine or plasma oxalate levels relative to pre-treatment baseline or improvement, stabilization, or slowed worsening of one or more clinical manifestations of PH1 (e.g., nephrocalcinosis, renal stone events, renal impairment, systemic oxalosis); AND
- (Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Dose will not exceed the FDA-labeled dose as described below:

Body weight	Maintenance Dose
Less than 10 kg	3 mg/kg once monthly
10 kg to less than 20 kg	6 mg/kg once every 3 months
20 kg and above	3 mg/kg once every 3 months

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When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of lumasiran (Oxlumo) when the patient has a secondary cause of hyperoxaluria or has received a liver transplant to be **not medically necessary**.**

Based on review of available data, the Company considers the continued use of lumasiran (Oxlumo) when the patient has not responded to therapy to be **not medically necessary**.**

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of lumasiran (Oxlumo) when patient selection criteria are not met (except those denoted above as **not medically necessary****) to be **investigational**.*

Background/Overview

Oxlumo is a small interfering RNA indicated for the treatment of patients with primary hyperoxaluria type 1 (PH1), a rare condition caused by a genetic mutation that results in buildup of oxalate. It works by targeting messenger RNA for the *hydroxyacid oxidase 1 (HAOI)* gene to reduce the production of glycolate oxidase and ultimately, oxalate. The dosing of Oxlumo is weight-based and consists of loading doses for the first 3 doses followed by maintenance doses either monthly or quarterly. It is administered as a subcutaneous injection by a healthcare professional. It should be noted that patients with end stage renal disease (ESRD) defined as an $eGFR \leq 30$ mL/min/1.73 m² were excluded from trials with this drug and thus the risks and benefits of Oxlumo to this population are unknown.

Primary hyperoxalurias are rare autosomal recessive inborn errors of glyoxylate metabolism that result in the overproduction of oxalate, primarily by the liver. PH1 is the most common form of primary hyperoxaluria with an estimated prevalence of 1-3 cases per 1 million individuals in the population. Each type of primary hyperoxaluria is caused by a different enzyme deficiency resulting from a specific mutation. PH1 results from mutations in the *AGXT* gene that encodes for a hepatic-

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specific peroxisomal enzyme, AGT. Clinical signs and symptoms of PH1 are caused by the buildup of oxalate and include progressive renal damage from tubular oxalate toxicity, nephrocalcinosis, and renal obstruction by stones, which are often accompanied by infection and inflammation. Ultimately, the patient's eGFR declines and the kidney becomes incapable of excreting all of the oxalate being produced. Plasma oxalate levels then rise and oxalate is deposited into a variety of tissues causing a range of effects depending on the tissue where the oxalate is deposited. Diagnosis is established by identification of biallelic pathogenic variants in *AGXT* on molecular genetic testing or via a liver biopsy to assay the activity of the AGT enzyme. Oxlumo is the first specific treatment for PH1. Prior to its approval, patients were encouraged to maintain a high fluid intake and limit oxalate-rich foods. Additional treatment options include oral potassium citrate or sodium citrate to alkalinize the urine and prevent calcium oxalate crystallization and pyridoxine supplementation to reduce oxalate synthesis.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Oxlumo was approved in November 2020 for the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary oxalate levels in pediatric and adult patients

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The safety and efficacy of Oxlumo was established based on two trials (ILLUMINATE-A and ILLUMINATE-B).

ILLUMINATE-A was a randomized, double-blind trial comparing Oxlumo and placebo in 39 patients 6 years of age and older with PH1 and an $\text{eGFR} \geq 30 \text{ mL/min/1.73m}^2$. Patients received 3 loading doses of 3 mg/kg Oxlumo (n=26) or placebo (n=13) administered once monthly, followed by quarterly maintenance doses of 3 mg/kg Oxlumo or placebo. The primary endpoint in the study was the percent reduction from baseline in 24-hour urinary oxalate excretion corrected for BSA

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averaged over months 3 through 6. The LS mean percent change from baseline in 24-hour urinary oxalate in the Oxlumo group was -65% (95% CI: -71, -59) compared with -12% (95% CI: -20, -4) in the placebo group, resulting in a between-group LS mean difference of 53% (95% CI: 45, 62).

ILLUMINATE-B was a single-arm study in 18 patients <6 years of age with PH1 and an eGFR>45 mL/min/1.73 m² or a normal serum creatinine for patients <12 months of age. Efficacy analyses included the first 16 patients who received 6 months of treatment with Oxlumo. Dosing was based on body weight. The primary endpoint was the percent reduction from baseline in spot urinary oxalate:creatinine ratio averaged over months 3 through 6. Patients treated with Oxlumo achieved a reduction in spot urinary oxalate:creatinine ratio from a baseline of 71%.

References

1. Oxlumo [package insert]. Alnylam Pharmaceuticals. Cambridge, MA. Updated November 2020.
2. Oxlumo Drug Evaluation. Express Scripts. Updated December 2020.

Policy History

Original Effective Date: 05/10/2021

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04/01/2021 Medical Policy Committee review

04/14/2021 Medical Policy Implementation Committee approval. New policy.

04/07/2022 Medical Policy Committee review

04/13/2022 Medical Policy Implementation Committee approval. No change to coverage.
Coding update

04/06/2023 Medical Policy Committee review

04/12/2023 Medical Policy Implementation Committee approval. No change to coverage.

Next Scheduled Review Date: 04/2024

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)[‡], copyright 2022 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of

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descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J0224
ICD-10 Diagnosis	All related diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

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- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
1. Consultation with technology evaluation center(s);
 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 3. Reference to federal regulations.

****Medically Necessary (or “Medical Necessity”)** - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and 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 that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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NOTICE: If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company

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recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

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