Medical Policy

Utilization Management and Clinical Medical Policy

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
lumasiran (Oxlumo®)	MP-RX-FP-196-26	☒ MMM MA ☒ MMM MultiHealth	10/21/2026 Last Review Date: 10/21/2026	10/21/2026 Frequently Revision: Annual

Service Category:

- ☐ Anesthesia
- ☐ Surgery
- ☐ Radiology Procedures
- ☐ Pathology and Laboratory Procedures
- ☐ Medicine Services and Procedures
- ☐ Evaluation and Management Services
- ☐ DME/Prosthetics or Supplies
- ☒ Other: Part B Drugs

Service Description:

This document addresses the use of Oxlumo (lumasiran), a HAO1-directed small interfering ribonucleic acid (siRNA) approved by the Food and Drug Administration (FDA) for the treatment for primary hyperoxaluria type 1 (PH1) to lower urinary and plasma oxalate levels in adult and pediatric individuals.

Background Information:

Oxlumo is intended for subcutaneous administration by a healthcare professional. The dosing schedule is based on actual body weight and includes three monthly loading doses followed by maintenance doses either monthly or every 3 months.

Primary hyperoxaluria (PH) is divided into three types, each caused by a mutation in a gene that encodes an enzyme that plays a role in glyoxylate metabolism. PH1 is the most common type, accounting for approximately 80% of PH cases. PH1 is caused by mutation in the AGXT gene which leads to decreased activity of the hepatic alanine:glyoxylate aminotransferase (AGT) enzyme. PH2 accounts for 10% of cases and is caused by mutation in the GRHPR gene, leading to decreased activity of the glyoxylate reductase/hydroxypyruvate reductase (GRHPR) enzyme. PH3 accounts for 5% of cases and is caused by mutation in the HOGA1 gene that encodes the mitochondrial 4-hydroxy-2-oxoglutarate aldolase enzyme. In individuals with increased urinary oxalate excretion, diagnosis is confirmed by genetic testing or liver biopsy showing decreased or absent enzyme activity.

Conservative management of PH1 should include high fluid intake (greater than 3 liters/1.73 m2 per day) to reduce oxalate deposition in the kidneys. Alkalinization of urine can also be beneficial to prevent urinary oxalate precipitation. Pyridoxine is a coenzyme of AGT that promotes the conversion of glyoxylate to glycine instead of oxalate. 30-50% of individuals with PH1 experience a significant reduction in hyperoxaluria in response to pyridoxine therapy. A trial of pyridoxine at a dose between 5 and 20 mg/kg per day is prudent in individuals with a pyridoxine-responsive genotype.

Oxlumo treats PH1 by decreasing levels of the glycolate oxidase (GO) enzyme in the liver, thereby reducing a substrate necessary for oxalate production. The GO enzyme is upstream of AGT, the enzyme that is deficient in PH1. Oxlumo is only expected to be effective in PH1 as it does not impact the metabolic pathways leading to hyperoxaluria in PH2 and PH3.

The clinical efficacy of Oxlumo was demonstrated in the ILLUMINATE clinical trial program. ILLUMINATE-A was a randomized, doubleblind, placebo-controlled trial in 39 individuals 6 years of age and older with PH1 and an estimated glomerular filtration rate (eGFR) ≥30 mL/min/1.73 m2. Individuals with a history of renal or liver transplant were excluded. The primary endpoint was the percent reduction in urinary oxalate excretion averaged over months 3 through 6. The mean percent change from baseline in urinary oxalate in the Oxlumo group was -65% compared with -12% in the placebo group ($p<0.0001$).

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
lumasiran (Oxlumo®)	MP-RX-FP-196-26	☒ MMM MA ☒ MMM MultiHealth	10/21/2026	10/21/2026
			Last Review Date: 10/21/2026	Frequently Revision: Annual

ILLUMINATE-B was a single-arm study in 18 individuals less than 6 years of age with PH1 and preserved renal function. Individuals with a history of renal or liver transplant were excluded. The primary endpoint was the percent reduction in spot urinary oxalate:creatinine ratio averaged over months 3 through 6. Individuals treated with Oxlumo demonstrated a reduction in spot urinary oxalate:creatinine ratio from baseline of 71%.

ILLUMINATE-C was a single-arm study in 21 individuals with PH1 and advanced kidney disease. Cohort A included 6 individuals who did not require dialysis at enrollment and cohort B included 15 individuals who were on a stable regimen of hemodialysis. The primary endpoint was the percent change in plasma oxalate averaged over months 3 through 6. Individuals treated with Oxlumo demonstrated a mean difference in plasma oxalate levels of -33% in cohort A and -42% in cohort B.

Approved Indications

A. For the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary and plasma oxalate levels in pediatric and adult patients.

Other Uses

A. None.

Medical Policy

Utilization Management and Clinical Medical Policy

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
lumasiran (Oxlumo®)	**MP-RX-FP-196-26**	☒ **MMM MA** ☒ **MMM MultiHealth**	**10/21/2026**	**10/21/2026**
			Last Review Date: **10/21/2026**	**Frequently Revision:** **Annual**

Medical Necessity Guidelines:

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

lumasiran (Oxlumo®)

A. Criteria For Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

Initial requests for Oxlumo (lumasiran) may be approved if the following criteria are met:

i. Individual has a diagnosis of primary hyperoxaluria type 1 (PH1); **AND**
ii. Documentation is provided that diagnosis has been verified by (Cochat 2012; Milliner 2022):
    A. Genetic testing demonstrating mutation in the alanine:glyoxylate aminotransferase (AGXT) gene; **OR**
    B. Liver biopsy demonstrating significantly decreased or absent alanine:glyoxylate aminotransferase (AGT) enzyme activity; **AND**
iii. Documentation is provided that individual has elevated urinary oxalate levels or plasma oxalate levels; **AND**
iv. Individual is using in combination with pyridoxine (unless individual is a pyridoxine non-responder) (Cochat 2012; Milliner 2022).

B. Criteria For Continuation of Therapy

Continuation requests for Oxlumo (lumasiran) may be approved if the following criteria are met:

i. Individual has a diagnosis of primary hyperoxaluria type 1 (PH1); **AND**
ii. Documentation is provided that diagnosis has been verified by (Cochat 2012; Milliner 2024):
    A. Genetic testing demonstrating mutation in the alanine:glyoxylate aminotransferase (AGXT) gene; **OR**
    B. Liver biopsy demonstrating significantly decreased or absent alanine:glyoxylate aminotransferase (AGT) enzyme activity; **AND**
iii. Documentation is provided that there is clinically significant reduction in urinary oxalate excretion, spot urinary oxalate:creatinine ratio or plasma oxalate levels) with Oxlumo therapy; A**ND**
iv. Individual is using in combination with pyridoxine (unless individual is a pyridoxine non-responder) (Cochat 2012; Milliner 2024).

C. Authorization Duration

i. Initial Approval Duration: Up to 6 months

Policy Name: lumasiran (Oxlumo®)	Policy Number: MP-RX-FP-196-26	Scope: ☒ MMM MA ☒ MMM MultiHealth	Origination Date: 10/21/2026	Effective Date: 10/21/2026
			Last Review Date: 10/21/2026	Frequently Revision: Annual

ii. Reauthorization Approval Duration: Up to 12 months

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

Oxlumo (lumasiran) may not be approved for the following:

i. Individual with primary hyperoxaluria type 2 or type 3; **OR**
ii. Individual with a history of or planned kidney or liver transplant (NCT 03681184, NCT 03905694, NCT 04152200); **OR**
iii. Use in combination with Rivfloza (nedosiran); **OR**
iv. May not be approved when the above criteria are not met and for all other indications.

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
lumasiran (Oxlumo®)	MP-RX-FP-196-26	☒ MMM MA ☒ MMM MultiHealth	10/21/2026	10/21/2026
			Last Review Date: 10/21/2026	Frequently Revision: Annual

Limits or Restrictions:

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Oxlumo® (lumasiran) injection: 94.5 mg/0.5 mL single dose vial

Body Weight	Loading Dose	Maintenance Dose (starting one month after the last loading dose)
less than 10 kg	6 mg/kg sc once monthly for 3 doses	3 mg/kg once monthly
10 kg to less than 20 kg	6 mg/kg sc once monthly for 3 doses	6 mg/kg once every 3 months (quarterly)
20 kg and above	3 mg/kg sc once monthly for 3 doses	3 mg/kg once every 3 months (quarterly)
Exceptions		
• None		

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
lumasiran (Oxlumo®)	MP-RX-FP-196-26	☒ MMM MA ☒ MMM MultiHealth	10/21/2026	10/21/2026
			Last Review Date: 10/21/2026	Frequently Revision: Annual

Codes Information:

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

ICD-10 Diagnostic Codes:

Codes	Description
E72.530	Primary hyperoxaluria, type 1

HCPCS Codes:

Codes	Description
J0224	Injection, lumasiran, 0.5 mg [Oxlumo]

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
lumasiran (Oxlumo®)	MP-RX-FP-196-26	☒ MMM MA ☒ MMM MultiHealth	10/21/2026	10/21/2026
			Last Review Date: 10/21/2026	Frequently Revision: Annual

Reference Information:

1. Alnylam Pharmaceuticals, Inc. Oxlumo® (lumasiran) prescribing information. Revised April 2025. Available at: https://www.alnylam.com/sites/default/files/pdfs/OXLUMO-Prescribing-Information.pdf. Accessed August 25, 2026.
2. Alnylam Pharmaceuticals. A study of lumasiran in infants and young children with primary hyperoxaluria type 1 (ILLUMINATE-B). NLM Identifier: NCT 03905694. Last updated: February 14, 2025. Available at: https://www.clinicaltrials.gov/ct2/show/NCT03905694?term=NCT03905694&draw=2&rank=1. Accessed: December 4, 2025.
3. Alnylam Pharmaceuticals. A study to evaluate lumasiran in children and adults in primary hyperoxaluria type 1 (ILLUMINATE-A). NLM Identifier: NCT 03681184. Last updated: August 12, 2024. Available at: https://www.clinicaltrials.gov/ct2/show/NCT03681184?term=03681184&draw=2&rank=1. Accessed: December 4, 2025.
4. Alynylam Pharmaceuticals. A study to evaluate lumasiran in patients with advanced primary hyperoxaluria type 1 (ILLUMINATE-C). NLM Identifier: NCT 04152200. Last updated: July 18, 2025. Available at: https://clinicaltrials.gov/ct2/show/NCT04152200. Accessed: December 4, 2025.
5. Cochat P, Hulton SA, Acquaviva C, et. al. Primary hyperoxaluria Type 1: indications for screening and guidance for diagnosis and treatment. Nephrol Dial Transplant. 2012 May;27(5):1729-36.
6. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: December 4, 2025.
7. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
8. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically.
9. Milliner DS, Harris PC, Sas DJ, et al. Primary Hyperoxaluria Type 1. 2002 Jun 19 [Updated 2024 Aug 15]. In: Adam MP, Everman DB, Mirzaa GM, et al., editors. GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1283/.
10. Niaudet P, Bacchetta J. Primary hyperoxaluria: Clinical features, diagnosis, and management. Last updated: September 30, 2025. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Accessed: December 4, 2025.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from the health plan.

© CPT Only – American Medical Association

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
lumasiran (Oxlumo®)	MP-RX-FP-196-26	☒ MMM MA ☒ MMM MultiHealth	10/21/2026	10/21/2026
			Last Review Date: 10/21/2026	Frequently Revision: Annual

Policy History:

Type of Review	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Policy Inception	Elevance Health's Medical Policy adoption.	10/15/2026	10/21/2026