Original Effective Date: 05/01/2021
Current Effective Date: 09/28/2022
Last P&T Approval/Version: 07/27/2022
Next Review Due By: 07/2023
Policy Number: C21126-A

Oxlumo (lumasiran)

PRODUCTS AFFECTED

Oxlumo (lumasiran)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive

DIAGNOSIS:
Primary hyperoxaluria type1 (PH1)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review

A. PRIMARY HYPEROXALURIA TYPE 1 (PH1):

1. Documented diagnosis of Primary hyperoxaluria with confirmed alanine-glyoxylate aminotransferase (AGXT) gene mutation OR Liver biopsy demonstrating significantly decreased or absent alanine: glyoxylate aminotransferase (AGT) enzyme activity [DOCUMENTATION REQUIRED]

NOTE: Oxlumo is not effective in primary hyperoxaluria type 2 (PH2) or type 3 (PH3) because its mechanism of action does not affect the metabolic pathways causing hyperoxaluria in PH2 and PH3

AND

2. Prescriber attests member has made efforts to increase fluid intake to at least 3 L/1.73 m2 per day
   AND
3. Documentation of concurrent use of pyridoxine or trial and failure of or intolerance to pyridoxine for at least 3 months with no significant improvement observed (e.g. <30% reduction in urine oxalate concentration after at least 3 months of therapy.)
   AND
4. Prescriber attests the member has an estimated glomerular filtration rate (eGFR) greater than or equal to 30 mL/min/1.73m2, does not have end-stage renal disease requiring dialysis and that the member has not had previous kidney or liver transplant
   AND
5. Laboratory documentation of member's baseline urinary oxalate level [DOCUMENTATION REQUIRED]
   AND
6. Documentation of member's current weight (within the last 30 days)

CONTINUATION OF THERAPY:

1. Prescriber attests to or clinical review has found no evidence of disease progression or unacceptable toxicity
   AND
2. Laboratory improvement or stabilization in urinary oxalate excretion from baseline. (Consideration for improvement as reaching near normal (<1mmol/1.73m^2 per day) urinary oxalate excretion.) [DOCUMENTATION REQUIRED]
   AND
3. Prescriber attests the member has an estimated glomerular filtration rate (eGFR) greater than or equal to 30 mL/min/1.73m2, does not have end-stage renal disease requiring dialysis and that the member has not had previous kidney or liver transplant
   AND
4. Documentation of member's current weight (within the last 30 days)

DURATION OF APPROVAL:
Initial authorization: 6 months, Continuation of Therapy:12 months

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a nephrologist, urologist or geneticist [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
None

QUANTITY:
Oxlumo (lumasiran) is available in single use vials [94.5 mg/0.5 mL vial]

Body Weight	Loading Dose	Maintenance Dose
Less than 10 kg	6 mg/kg once monthly x 3 doses	3 mg/kg once monthly
10 kg to < 20 kg	6 mg/kg once monthly x 3 doses	6 mg/kg once every 3 months
20 kg and above	3 mg/kg once monthly x 3 doses	3 mg/kg once every 3 months

PLACE OF ADMINISTRATION:

The recommendation is that injectable medications in this policy will be for pharmacy or medical benefit coverage and the subcutaneous injectable products administered in a place of service that is a non-hospital facility-based location.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Subcutaneous

DRUG CLASS:
Hyperoxaluria Agents

FDA-APPROVED USES:
Indicated for the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary oxalate levels in pediatric and adult patients

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Oxlumo (lumasiran) is the first agent approved by the Food and Drug Administration (FDA) for the treatment for primary hyperoxaluria type 1 (PH1) to lower urinary oxalate levels in adult and pediatric individuals.
Primary hyperoxaluria is a rare inherited error of glyoxylate metabolism characterized by an excess production of oxalate. The excess oxalate is excreted by the kidneys, typically at a rate greater than 1 mmol/1.73 m2 per day (normal is less than 0.5 mmol/1.73 m2 per day). Increased urinary excretion of oxalate leads to urolithiasis and nephrocalcinosis. Progressive disease can result in end-stage kidney disease and systemic oxalate deposition.
Primary hyperoxaluria (PH) is divided into three primary 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. Neutral phosphate (orthophosphate), potassium citrate-citric acid and/or magnesium oxide 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. Up to 30% of individuals with PH1 experience a significant reduction in hyperoxaluria in response to pyridoxine therapy. A three to six-month trial of pyridoxine at a dose between 5 and 20 mg/kg per day is prudent in all individuals with PH1.

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, double blind, 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 ($p<0.0001$).

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 is an ongoing clinical trial in individuals with advanced PH1, including individuals with severe renal impairment and those on dialysis.
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

Currently, there are no other FDA-approved treatments for PH1. Conservative management includes increasing fluid intake to 3 L/m2 BSA per day to create a high urinary output following diagnosis; this is the most effective therapy to decrease tubular fluid oxalate concentration and intratubular oxalate deposition. In addition, pyridoxine should be tried for at least 3 months in all patients with PH1, as those who respond to therapy see a significant reduction in urinary oxalate excretion that is maintained for years.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Oxlumo (Lumasiran) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. No specific contraindications or warnings to Oxlumo (Lumasiran) have been identified.

OTHER SPECIAL CONSIDERATIONS:
None

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Solution, Subcutaneous injection: 94.5mg/0.5ml in a single-dose vial

REFERENCES

1. Oxlumo (lumasiran) [prescribing information]. Cambridge, MA: Alnylam Pharmaceuticals; November 2020.
2. Genetic and Rare Diseases Information Center. Primary hyperoxaluria type 1. https://rarediseases.info.nih.gov/diseases/2835/primary-hyperoxaluria-type-1 Updated November 8, 2021. Accessed May 2022.
3. National Institutes of Health. In NIH trial, A Study to Evaluate Lumasiran in Children andAdults with Primary Hyperoxaluria Type 1 (ILLUMINATE-A, NCT03681184). www.clinicaltrials.gov. Published September 2018. Updated January 2021.
4. National Institutes of Health. In NIH trial, A Study to Evaluate Lumasiran in Infants andYoung Children with Primary Hyperoxaluria Type 1 (ILLUMINATE-B, NCT03905694). www.clinicaltrials.gov. Published April 2019. Updated January 2021.
5. National Institutes of Health. In NIH trial, A Study to Evaluate Lumasiran in Patients with Advanced Primary Hyperoxaluria Type 1 (ILLUMINATE-C, NCT04152200). www.clinicaltrials.gov. Published November 2019. Updated January 2021.
6. National Institutes of Health. In NIH trial, Long Term Extension Study in Patients with Primary Hyperoxaluria (PHYOX3, NTC04042402). www.clinicaltrials.gov. Published August 2019. Updated February 2021.
7. Bhasin B, Urekli HM, Atta MG. Primary and secondary hyperoxaluria: understanding the enigma. World J Nephrol. 2015;4(2):235-244. doi:10.5527/wjn.v4.i2.235

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Prescriber Requirements References	Q3 2022
Q2 2022 Established tracking in new format	Historical changes on file