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Section:	Prescription Drugs	**Effective Date:**	July 1, 2025
Subsection:	Genitourinary Agents	**Original Policy Date:**	December 18, 2020
Subject:	Oxlumo	**Page:**	1 of 5

Last Review Date: June 12, 2025

Oxlumo

Description

Oxlumo (lumasiran)

Background
Oxlumo (lumasiran) targets oxalate overproduction in the liver. Primary hyperoxaluria type 1 (PH1) is a progressive genetic disease caused by mutations in the *AGXT* gene that render the liver enzyme alanine:glyoxylate aminotransferase (AGT) dysfunctional. Normally, AGT processes glyoxylate, which is generated by another liver enzyme, glycolate oxidase (GO). In PH1, a defect in AGT means glyoxylate is instead converted to oxalate. Oxalate cannot be metabolized and is typically excreted by the kidneys at normal levels. When overproduced as it is in PH1, oxalate can cause progressive, irreversible damage. Oxalate combines with calcium, creating calcium oxalate crystals leading to kidney stones and crystal deposits throughout the body. Oxlumo is not expected to be effective in primary hyperoxaluria type 2 (PH2) or type 3 (PH3) because its mechanism of action does not affect the metabolic pathways causing PH2 and PH3 (1-2).

Regulatory Status
FDA-approved indication: Oxlumo is a *HAO1*-directed small interfering ribonucleic acid (siRNA) indicated for the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary and plasma oxalate levels in pediatric and adult patients (1).

Oxlumo is intended for subcutaneous use and should be administered by a healthcare professional. The recommended dosing regimen of Oxlumo consists of loading doses followed

by maintenance doses administered subcutaneously. Dosing is based on actual body weight (1).

The most common adverse reaction is injection site reactions (1).

The safety and effectiveness of Oxlumo have been established in pediatric patients aged birth and older (1).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Oxlumo may be considered **medically necessary** if the conditions indicated below are met.

Oxlumo may be considered **investigational** for all other indications.

Prior-Approval Requirements

Diagnosis

Patient must have the following:

Primary hyperoxaluria type 1 (PH1)

AND ALL of the following:

a. Diagnosis confirmed by identification of biallelic pathogenic variants in alanine:glyoxylate aminotransferase (*AGT* or *AGXT*) gene **OR** liver biopsy demonstrating AGT deficiency
b. Presence of 1 of the following clinical signs or symptoms of PH1:
    i. Elevated urine oxalate excretion (body surface area-normalized daily urine oxalate excretion output ≥ 0.7 mmol/1.73 m^2)
    ii. Elevated plasma oxalate concentration > 20 µmol/L or > 1.76 mg/L
    iii. Urine oxalate excretion:creatinine ratio above age-specific upper limit of normal
c. Patient has not received a liver transplant
d. Prescribed by or in consultation with a nephrologist, urologist, geneticist, or any healthcare provider with expertise in treating primary hyperoxaluria type 1

e. Patient will be dosed based on actual body weight
f. Prescriber agrees to monitor urinary **OR** plasma oxalate levels

Prior – Approval *Renewal* Requirements

Diagnosis

Patient must have the following:

Primary hyperoxaluria type 1 (PH1)

AND ALL of the following:

a. Patient has had a clinically meaningful response to therapy from pre-treatment baseline (e.g., decreased urinary oxalate concentrations, decreased urinary oxalate:creatinine ratio, decreased plasma oxalate concentrations, improvement, stabilization or slowed worsening of nephrocalcinosis, renal stone events, renal impairment, or systemic calcinosis)
b. Patient has not received a liver transplant
c. Patient will be dosed based on actual body weight

Policy Guidelines

Pre – PA Allowance

None

Prior - Approval Limits

Duration 6 months

Prior – Approval *Renewal* Limits

Duration 12 months

Rationale

Summary

Oxlumo (lumasiran) reduces levels of glycolate oxidase (GO) enzyme by targeting the hydroxyacid oxidase 1 (*HAO1*) messenger ribonucleic acid (mRNA) in hepatocytes through RNA interference. Decreased GO enzyme levels reduce the amount of available glyoxylate, a

substrate for oxalate production. The safety and effectiveness of Oxlumo have been established in pediatric patients aged birth and older (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Oxlumo while maintaining optimal therapeutic outcomes.

References

1. Oxlumo [package insert]. Cambridge, MA: Alnylam Pharmaceuticals, Inc.; April 2025.
2. Cochat P, Rumsby G. *N Engl J Med*. 2013;369(7):649-658. Accessed on November 6, 2023.

Policy History

Date	Action
December 2020	Addition to PA
March 2021	Annual editorial review Revised background and summary sections per SME
August 2022	Per FEP/Association policy, revised criteria to align with BCBSA Pharmacy and Therapeutics committee policy. For initiation: added requirement diagnosis confirmed by identification of biallelic pathogenic variants in alanine:glyoxylate aminotransferase (*AGT or AGXT*) gene **OR** liver biopsy demonstrating AGT deficiency; presence of 1 of the following clinical signs or symptoms of primary hyperoxaluria type 1: i. Elevated urine oxalate excretion (body surface area-normalized daily urine oxalate excretion output ≥ 0.7 mmol/1.73 m2) ii. Elevated plasma oxalate concentration > 20 µmol/L or > 1.76 mg/L iii. Urine oxalate excretion:creatinine ratio above age-specific upper limit of normal; patient has not received a liver or kidney transplant; eGFR > 30 mL/min/1.73^2; Prescribed by or in consultation with a nephrologist, urologist, geneticist, or any healthcare provider with expertise in treating primary hyperoxaluria type 1. For continuation: Added b. Patient has had a clinically meaningful response to therapy from pre-treatment baseline (e.g., decreased urinary oxalate concentrations, decreased urinary oxalate:creatinine ratio, decreased plasma oxalate concentrations, improvement, stabilization or slowed worsening of nephrocalcinosis, renal stone events, renal impairment or systemic calcinosis) Urinary oxalate levels have decreased; c. Patient has not received a liver or kidney transplant
September 2022	Annual review

June 2023	Annual editorial review and reference update. Per SME, removed requirement to not have had a kidney transplant in both initiation and continuation requirements
September 2023	Association policy alignment: removed eGFR requirement, added requirement of monitoring plasma oxalate levels, and changed duration of initiation approval to 6 months from 12 months
December 2023	Annual review and reference update
June 2024	Annual review
June 2025	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 12, 2025 and is effective on July 1, 2025.