CarePartners of Connecticut MEDICARE ADVANTAGE

Medical Necessity Guidelines
Medical Benefit Drugs
Oxlumo® (lumasiran)

Effective: May 1, 2024

Guideline Type	☒ Prior Authorization ☐ Non-Formulary ☐ Step-Therapy ☐ Administrative

Applies to:

☒ CarePartners of Connecticut Medicare Advantage HMO plans, Fax 617-673-0956
☒ CarePartners of Connecticut Medicare Advantage PPO plans, Fax 617-673-0956

Note: While you may not be the provider responsible for obtaining prior authorization, as a condition of payment you will need to ensure that prior authorization has been obtained.

Overview

Primary hyperoxaluria type 1 (PH1) is a rare genetic disease caused by hepatic overproduction of oxalate that leads to kidney stones, nephrocalcinosis, kidney failure, and systemic oxalosis. The metabolic defect in PH1 results from a deficiency of the liver-specific peroxisomal enzyme alanine-glyoxylate aminotransferase (AGT), which converts the oxalate precursor glyoxylate to glycine. With absent or deficient AGT activity, glyoxylate is oxidized to oxalate, leading to increased plasma oxalate levels.

A diagnosis of PH1 is confirmed by genetic testing for the alanine:glyoxylate aminotransferase (AGXT) gene mutation. If no mutation is found, then AGT activity can be evaluated via a liver biopsy to determine reduced or absent enzyme activity.

Since data have established that urinary oxalate levels in PH1 are a primary determinant of progression to end-stage kidney disease, management of the condition is directed toward reducing urinary oxalate levels.

Oxlumo (lumasiran) works in PH1 by reducing hepatic oxalate production and increases concentrations of a readily excreted precursor, glycolate, by degrading the messenger RNA that encodes glycolate oxidase, an enzyme upstream of AGT. This mechanism is not expected to reduce hepatic oxalate production to the same extent in patients with the non-PH1 genetic causes of primary hyperoxaluria, PH2 or PH3. Approval of Oxlumo was based on the placebo-controlled ILLUMINATE-A and open-label ILLUMINATE-B trials which included a combined 57 patients with PH1. Patients who received Oxlumo saw a reduction in urinary oxalate versus placebo. The ILLUMINATE-C trial is a single arm, open-label trial in patients with advanced PH1, including those receiving hemodialysis. Results demonstrated that regardless of hemodialysis status, treatment with Oxlumo had positive results on the percent change in plasma oxalate from baseline.

Food and Drug Administration - Approved Indications

Oxlumo (lumasiran) is a *HAO1*-directed small interfering ribonucleic acid (siRNA) indicated for the treatment of PH1 to lower urinary oxalate levels and plasma oxalate levels in pediatric and adult patients.

Clinical Guideline Coverage Criteria

The plan may authorize coverage for Oxlumo for Members when all of the following criteria are met:

Initial Authorization Criteria

1. Documented diagnosis of primary hyperoxaluria type 1 confirmed by **one (1)** of the following:
    a. Molecular genetic test showing a mutation in the alanine:glyoxylate aminotransferase (AGXT) gene
    b. Liver enzyme analysis demonstrating absent or significantly reduced alanine: glyoxylate aminotransferase (AGT) activity

AND

2. Prescribed by, or in consultation with, an endocrinologist, nephrologist or a specialist with experience managing primary hyperoxaluria

AND

3. Documentation the patient has not had a liver transplantation

Reauthorization Criteria

1. Documented diagnosis of primary hyperoxaluria type 1 confirmed by **one (1)** of the following:
    a. Molecular genetic test showing a mutation in the alanine: glyoxylate aminotransferase (AGXT) gene
    b. Liver enzyme analysis demonstrating absent or significantly reduced alanine: glyoxylate aminotransferase (AGT) activity.

AND

2. Prescribed by, or in consultation with, an endocrinologist, nephrologist or a specialist with experience managing primary hyperoxaluria

AND

3. Documentation the patient has not had a liver transplantation

AND

4. Documentation of a positive clinical response as evidenced by at least **one (1)** of the following:
    a. Decreased or normalized urinary oxalate concentration compared to pre-treatment baseline
    b. Decreased or normalized plasma oxalate concentration compared to pre-treatment baseline

Limitations

- The Plan will not cover Oxlumo in Members with primary hyperoxaluria type 2 or type 3.
- Authorizations for Oxlumo will be provided in 12-month intervals.
- Patients new to the plan stable on Oxlumo should be reviewed against Reauthorization Criteria.

Codes

The following code(s) require prior authorization:

Table 1: HCPCS Codes

HCPCS Codes	Description
J0224	Injection ferric lumasiran, .5mg

References:

1. 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; 27(5):1729-36.
2. Garrelfs SF, et al. Lumasiran, an RNAi Therapeutic for Primary Hyperoxaluria Type 1. N Engl J Med. 2021;384:1216-1226.
3. Hoppe B, Beck BB, Milliner DS. The primary hyperoxalurias. Kidney Int 2009; 75:1264.
4. Bhasin B, et al. Primary and secondary hyperoxaluria: understanding the enigma. World J Nephrol. 2015;4(2):235-44.
5. Oxlumo (lumasiran) [prescribing information]. Cambridge, MA: Alnylam Pharmaceuticals, Inc.; September 2023.

Approval And Revision History

April 19, 2023: year: Reviewed by the Medical Policy Approval Committee (MPAC).

May 9, 2023: Reviewed by Pharmacy and Therapeutics Committee (P&T).

Subsequent endorsement date(s) and changes made:

- Originally approved September 13, 2022 by P&T and September 21, 2022 by MPAC committees effective January 1, 2023.
- Administrative update: April 2023 added Medical Benefit Drugs to title and CPCT logo update.
- May 17, 2023: Annual review added “and plasma oxalate levels in” to FDA approved indications in overview effective July 1, 2023.
- November 2023: Administrative Update in support of calendar year 2024 Medicare Advantage and PDP Final Rule.
- November 2023: Administrative Update in support of calendar year 2024 Medicare Advantage and PDP Final Rule.
- February 13, 2024: Added Reauthorization Criteria to the Medical Necessity Guideline. Added confirmation of a diagnosis of PH1 by either genetic testing or liver enzyme results. Added the requirement that the patient has not had a liver transplantation. Added Limitations to support approval durations and how patients new to the plan stable on the

requested medication should be reviewed. Removed the Limitation Any indications other than those listed are considered experimental or investigational and will not be approved by the Plan. Minor wording updates (eff 5/1/2024).

Background, Product and Disclaimer Information

Point32Health prior authorization criteria to be applied to Medicare Advantage plan members is based on guidance from Medicare laws, National Coverage Determinations (NCDs) or Local Coverage Determinations (LCDs). When no guidance is provided, Point32Health uses clinical practice guidance published by relevant medical societies, relevant medical literature, Food and Drug Administration (FDA)-approved package labeling, and drug compendia to develop prior authorization criteria to apply to Medicare Advantage plan members. Medications that require prior authorization generally meet one or more of the following criteria: Drug product has the potential to be used for cosmetic purposes; drug product is not considered as first-line treatment by medically accepted practice guidelines, evidence to support the safety and efficacy of a drug product is poor, or drug product has the potential to be used for indications outside of the indications approved by the FDA. Prior authorization and use of the coverage criteria within this Medical Necessity Guideline will ensure drug therapy is medically necessary, clinically appropriate, and aligns with evidence-based guidelines. We revise and update Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests revisions.

Treating providers are solely responsible for the medical advice and treatment of Members. The use of this guidelines not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to eligibility and benefits on the date of service, coordination of benefits, referral/authorization, utilization management guidelines when applicable, and adherence to plan policies, plan procedures, and claims editing logic.