DRUG DETERMINATION POLICY

Title: DDP-51 Oxlumo

Effective Date: 06/01/2021

Physicians Health Plan
PHP Insurance Company
PHP Service Company

Important Information - Please Read Before Using This Policy

The following policy applies to health benefit plans administered by PHP and may not be covered by all PHP plans. Please refer to the member's benefit document for specific coverage information. If there is a difference between this general information and the member's benefit document, the member's benefit document will be used to determine coverage. For example, a member's benefit document may contain a specific exclusion related to a topic addressed in a coverage policy.

Benefit determinations for individual requests require consideration of:

1. The terms of the applicable benefit document in effect on the date of service.
2. Any applicable laws and regulations.
3. Any relevant collateral source materials including coverage policies.
4. The specific facts of the particular situation.

Contact PHP Customer Service to discuss plan benefits more specifically.

1.0 Policy:

This policy describes the determination process for coverage of specific drugs that require prior approval.

This policy does not guarantee or approve benefits. Coverage depends on the specific benefit plan. Drug Determination Policies are not recommendations for treatment and should not be used as treatment guidelines.

2.0 Background or Purpose:

Oxlumo, a gene silencer on hydroxyacid oxidase 1 mRNA, is a specialty drug used to lower urinary oxalate levels in adults and children with type 1 primary hyperoxaluria. Type 1 primary hyperoxaluria is caused by a defect in the gene that encodes AGT, a hepatic enzyme responsible in breaking down oxalate. It is the most common form of primary hyperoxaluria that accounts for about 70 to 80 percent of all reported cases. High oxalate levels can cause kidney stones, renal inflammation, and fibrosis. If persistent and left untreated, it can lead to end-stage renal disease. These criteria were developed and implemented to ensure appropriate use for the intended diagnosis, if possible.

3.0 Clinical Determination Guidelines:

Document the following with chart notes:

I. Type 1 Primary Hyperoxaluria [must meet all listed below]:

   A. Prescriber: nephrologist.

   B. Diagnosis and severity.

      1. Type 1 Primary Hyperoxaluria [must meet all listed below]:

         a. Signs and symptoms including recurrent kidney stones, urolithiasis, infantile oxalosis, renal failure, nephrocalcinosis with decreased glomerular filtration rate (GFR), presence of oxalate crystals or stones.

b. Genetic testing that confirmed homozygous or compound heterozygous AGXT mutation.

2. Documentation of laboratory levels confirming Type 1 Primary Hyperoxaluria [must meet one listed below]:

a. Urine oxalate greater than the upper limit of normal (refer to Appendix II).

b. Urine oxalate/creatinine greater than the normal range based on patient's age (refer to Appendix II).

C. Dosage and administration.

1. Loading dose:

a. Below 20kg: 6mg per kilogram (kg) subcutaneous injection once monthly for three doses.

b. At or above 20kg: 3mg per kg subcutaneous injection once monthly for three doses.

2. Maintenance dose:

a. Below 10kg: 3mg per kg subcutaneous injection once monthly.

b. At or above 10 to below 20kg: 6mg per kg subcutaneous injection once every three months.

c. Above 20kg: 3mg per kg subcutaneous injection once every three months.

D. Approval.

1. Initial: six months.

2. Re-approval: six months [must meet all listed below]:

a. Improvement in urine oxalate level and/or urine oxalate - creatinine ratio from baseline.

b. Documentation of reduced signs and symptoms of type 1 primary hyperoxaluria.

II. Appropriate medication use [must meet all listed below]:

A. Diagnosis: meets standard diagnostic criteria that designates signs, symptoms and test results to support specific diagnosis.

B. FDA approval status [must meet one listed below]:

1. FDA approved: product, indication, and/or dosage regimen.

2. Off-label use: at least two supporting studies from major peer-reviewed medical journals that support the off-label use as safe and effective.

C. Place in therapy: sequence of therapy supported by national or international accepted guidelines and/or studies (e.g., oncologic, infectious conditions.

III. Exclusions for any of the following conditions:

A. Secondary causes of hyperoxaluria including excessive dietary consumption of oxalate, gastric bypass surgery, inflammatory bowel disease, or other intestinal disorders.

B. Patient underwent or scheduled to have a liver and/or kidney transplant.

4.0 Coding:

CODES AFFECTED				
Code	**Brand**	**Generic**	**Billing (1u)**	**Prior Approval Required**
J0224	Oxlumo	lumasiran	94.5mg/0.5mL	Y

5.0 References, Citations & Resources:

1. Lexicomp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Oxlumo accessed February 2021.
2. Liebow A, Li X, Racie T, et al. An investigational RNAi therapeutic targeting glycolate oxidase reduces oxalate production in models of primary hyperoxaluria. J Am Soc Nephrol. 2017;28:494-503.
3. Oxlumo [prescribing information]. Cambridge, MA: Alnylam Pharms, Inc.; November 2020.
4. Hoppe, B., 2012. An update on primary hyperoxaluria. Nature Reviews Nephrology, 8(8), pp.467-475.
5. Sas, D., Enders, F., Mehta, R., Tang, X., Zhao, F., Seide, B., Milliner, D. and Lieske, J., 2020. Clinical features of genetically confirmed patients with primary hyperoxaluria identified by clinical indication versus familial screening. Kidney International, 97(4), pp.786-792.

6.0 Appendices:

See page 4.

7.0 Revision History:

Original Effective Date: 06/01/2021

Next Review Date: 03/24/2022

Revision Date	Reason for Revision
9/21	Code changed for Oxlumo

Appendix I: Patient Safety and Monitoring

Drug	Adverse Reactions	Monitoring	REMS
Oxlumo (lumasiran)	• Gastrointestinal: abdominal pain (15%) • Dermatologic: injection site reaction (38%)	• Urinary oxalate levels	N/A

Appendix II: Laboratory Levels Confirming Type 1 Primary Hyperoxaluria

	Normal Reference Levels
Urinary Oxalate	<45 mg/1.73 m^2/day
Urinary Oxalate/Creatinine	
0-6 months of age	<0.175 mg/mg
6-12 months of age	<0.139 mg/mg
1-2 years of age	<0.103 mg/mg
2-3 years of age	<0.080 mg/mg
3-5 years of age	<0.064 mg/mg
5-7 years of age	<0.056 mg/mg
7-17 years of age	<0.048 mg/mg

Appendix III: Differential Diagnosis Based on Genetic Testing

Type of Primary Hyperoxaluria	Genetic Testing Results
Type 1	Defects in the gene that encodes the hepatic peroxisomal enzyme alanine: glyoxylate aminotransferase (AGT)
Type 2	Defects in the gene that encodes the cytosolic enzyme glyoxylate reductase/hydroxypyruvate reductase (GRHPR)
Type 3	Defects in the HOGA1 gene that encodes the liver-specific mitochondrial 4-hydroxy-2-oxoglutarate aldolase enzyme