Drug Coverage Policy

Effective Date.....06/01/2024
Coverage Policy Number.....IP0629
Policy Title.....Rivfloza

Metabolic Disorders – Primary Hyperoxaluria Medications – Rivfloza

- Rivfloza™ (nedosiran subcutaneous injection – Novo Nordisk)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna Healthcare Coverage Policy

Overview

Rivfloza, a lactate dehydrogenase A-directing (LDHA) small interfering RNA, is indicated for the treatment of **primary hyperoxaluria type 1** (PH1) to lower urinary and plasma oxalate levels in adults and children ≥ 9 years of age with relatively preserved kidney function.[1]

Disease Overview

Primary hyperoxaluria type 1 is a rare autosomal recessive inborn error of glyoxylate metabolism that results in the overproduction of oxalate, which forms insoluble calcium oxalate crystals that accumulate in the kidney and other organs, leading to issues such as nephrocalcinosis, formation of

renal stones, and renal impairment.[2] Mutations in the alanine: glyoxylate aminotransferase gene (AGXT) cause primary hyperoxaluria type 1.[3] Liver transplantation is the only curative intervention for primary hyperoxaluria type 1 as it corrects the underlying enzymatic defect due to mutations of the AGXT gene.[2-4]

Clinical Efficacy
The efficacy of Rivfloza for the treatment of primary hyperoxaluria type 1 has been evaluated in one pivotal study.[1,5] The study included patients ≥ 9 years of age with genetically confirmed PH1 and urinary oxalate excretion ≥ 0.7 mmol/24 hr/1.73 m^2. An ongoing open-label extension trial is following patients for up to 4 years.[6] The primary efficacy endpoint of the area under the curve (AUC) percent change from baseline in 24-hour urinary oxalate excretion was assessed following 6 months of Rivfloza therapy.

Dosing
Dosing of Rivfloza is a weight-based monthly subcutaneous injection.[1]

Table 1. Rivfloza Dosing Regimen.[1]

Age	Body Weight	Dosing Regimen
Adults and adolescents ≥ 12 years of age	≥ 50 kg	160 mg once monthly
	< 50 kg	128 mg once monthly
Children 9 to 11 years of age	≥ 50 kg	160 mg once monthly
	< 50 kg	3.3 mg/kg once monthly, not to exceed 128 mg

Medical Necessity Criteria

Rivfloza is considered medically necessary when the following is met:

FDA-Approved Indication

1. **Primary Hyperoxaluria Type 1.** Approve Rivfloza for the duration noted if the patient meets one of the following (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets the following (i, ii, iii, iv, v, vi, and vii):
     - **i.** Patient is ≥ 9 years of age; AND
     - **ii.** Patient has had a genetic test confirming the diagnosis of Primary Hyperoxaluria Type 1 via identification of an alanine: glyoxylate aminotransferase gene (AGXT) mutation ; AND
     - **iii.** Patient has an estimated glomerular filtration rate (eGFR) ≥ 30 ml/min per 1.73 m^2; AND
     - **iv.** Patient meets ONE of the following (a, b, or c):
       - **a)** Patient has a urinary oxalate excretion ≥ 0.7 mmol/24 hours/1.73 meters^2; OR
       - **b)** Patient has a urinary oxalate: creatinine ratio above the age-specific upper limit of normal; OR
       - **c)** Patient has a plasma oxalate level ≥ 20 µmol/L; AND
     - **v.** Patient has not previously received a liver transplant for Primary Hyperoxaluria Type 1; AND
     - **vi.** The medication is prescribed by or in consultation with a nephrologist or urologist.
     - **vii.** Preferred product criteria is met for the product(s) as listed in the below table(s)

B) Patient is Currently Receiving Rivfloza. Approve for 1 year if, according to the prescriber, the patient is continuing to derive benefit from Rivfloza as determined by the most recent (i.e., within the past 6 months) objective measurement.
Note: Examples of objective measurements of a response to Rivfloza therapy are reduced urinary oxalate excretion, decreased urinary oxalate: creatinine ratio, or reduced plasma oxalate levels from baseline (i.e., prior to Rivfloza therapy) or improved or stabilized clinical signs/symptoms of Primary Hyperoxaluria Type 1 (e.g., nephrocalcinosis, formation of renal stones, renal impairment).

Dosing. Approve the following dosing regimens.

- **i.** If weight is ≥ 50 kg, approve for 160mg once monthly.
- **ii.** If weight is < 50 kg, approve 3.3 mg/kg once monthly, not to exceed 128mg.

Employer Plans:

Product	Criteria
Rivfloza (nedosiran subcutaneous injection)	ONE of the following (1 or 2): 1. The patient has tried and, according to the prescriber, has experienced inadequate efficacy OR significant intolerance with Oxlumo. 2. The patient has already been started on therapy with Rivfloza.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Primary Hyperoxaluria Type 2 (PH2).** Rivfloza may have benefit in PH2; however, the efficacy and safety of Rivfloza in patients with PH2 have not been established. Clinical trials are ongoing.

2. **Primary Hyperoxaluria Type 3 (PH3).** Rivfloza may have benefit in PH3; however, the efficacy and safety of Rivfloza in patients with PH3 have not been established. Clinical trials are ongoing.

3. **Primary Hyperoxaluria with end stage renal disease (ESRD).** Rivfloza may have benefit in patients with PH1 or PH2 and ESRD; however, the efficacy and safety of Rivfloza in this patient population have not been established. Clinical trials are ongoing.

4. **Concurrent use of Rivfloza with Oxlumo (lumasiran subcutaneous injection).** Oxlumo is another small interfering RNA agent and should not be used with Rivfloza.

Coding Information

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.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J3490	Unclassified drugs

References

1. Rivfloza™ subcutaneous injection [prescribing information]. Plainsboro, NJ: Novo Nordisk; September 2023.
2. Milliner DS, Harris PC, Sas DJ, et al. Primary Hyperoxaluria Type 1. Gene Reviews® Available at: https://www.ncbi.nlm.nih.gov/books/NBK1283/#:~:text=In%20primary%20hyperoxaluria%20type%201,deposit%20in%20the%20renal%20parenchyma. Updated February 10, 2022. Accessed on October 3, 2023.
3. Primary Hyperoxaluria: MedlinePlus Genetics. U.S. National Library of Medicine; National Institutes of Health; Department of Health and Human Services. Available at: https://medlineplus.gov/genetics/condition/primary-hyperoxaluria/#resources. Accessed on October 3, 2023.
4. Cochat P, Rumsby G. Primary hyperoxaluria. *N Engl J Med*. 2013;369(7):649-658.
5. Baum MA, Langman C, Cochat P, et al. PHYOX2: a pivotal randomized study of nedosiran in primary hyperoxaluria type 1 or 2. *Kidney Int.* 2023;103(1):207-217.
6. Hoppe B, Coenen M, Schalk G, et al. Nedosiran in primary hyperoxaluria subtype 1: interim results from an open label extension trial (PHYOX3) [poster]. Presented at: 19th International Pediatric Nephrology Association (IPNA) Congress. Calgary, Canada. September 7-11, 2022.

Revision Details

Type of Revision	Summary of Changes	Date
New	New policy	06/01/2024

The policy effective date is in force until updated or retired