



PRIOR AUTHORIZATION POLICY

- POLICY:** Metabolic Disorders – Primary Hyperoxaluria Medications – Rivfloza Prior Authorization Policy
- Rivfloza™ (nedosiran subcutaneous injection – Novo Nordisk)

REVIEW DATE: 11/22/2023

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 NATIONAL FORMULARY COVERAGE:

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 m². 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.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Rivfloza. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Rivfloza as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Rivfloza to be prescribed by or in consultation with a physician who specializes in the condition being treated. All reviews will be forwarded to the Medical Director for evaluation.

Documentation: Documentation is required for use of Rivfloza as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory tests, claims records, and/or other information. Subsequent coverage reviews for a patient who has previously met the documentation requirements and related criteria in the Rivfloza *Prior Authorization Policy* through the Coverage Review Department, and who is requesting reauthorization, are NOT required to re-submit documentation for reauthorization, except for the criterion requiring documentation of a continued benefit from Rivfloza therapy.

• **Rivfloza™ (nedosiran subcutaneous injection – Novo Nordisk) is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):**

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, and vi):

- 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 **[documentation required]**; AND
- iii.** Patient has an estimated glomerular filtration rate (eGFR) ≥ 30 ml/min per 1.73 m² **[documentation required]**; 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 meters² **[documentation required]**; OR
 - b) Patient has a urinary oxalate:creatinine ratio above the age-specific upper limit of normal **[documentation required]**; OR
 - c) Patient has a plasma oxalate level ≥ 20 $\mu\text{mol/L}$ **[documentation required]**; 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.
- 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 **[documentation required]**.
- 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).

CONDITIONS NOT COVERED

• **Rivfloza™ (nedosiran subcutaneous injection – Novo Nordisk) is(are) considered experimental, investigational or unproven for ANY other use(s) 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.

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.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy		11/22/2023

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