

Rivfloza® (Nedosiran) (for Indiana Only)

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[Instructions for Use](#)

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| Related Policies |
|------------------|
| None |

Application

This Medical Benefit Drug Policy only applies to the state of Indiana.

Coverage Rationale

This policy provides information about the use of certain specialty pharmacy medications administered by either the subcutaneous (SC) or intravenous (IV) route by a healthcare professional (HCP)

Rivfloza for provider administration is proven and medically necessary for the treatment of PH1 in patients who meet all of the following criteria:

- For **initial therapy**, all of the following:
 - Diagnosis of PH1 by, or in consultation with, a specialist (e.g., geneticist, nephrologist, urologist) with expertise in the diagnosis of PH1; **and**
 - Confirmation of the PH1 diagnosis based on **both** of the following:
 - § Metabolic testing demonstrating **one** of the following:
 - Increased urinary oxalate excretion [e.g. greater than 1 mmol/1.73 m2 per day (90 mg/1.73 m2 per day), increased urinary oxalate:creatinine ratio relative to normative values for age]; **or**
 - Increased plasma oxalate and glyoxylate concentrations
 - and**
 - § Genetic testing has confirmed a mutation in the alanine: glyoxylate aminotransferase (AGT or AGXT) gene
 - and**
 - Patient has not received a liver transplant; **and**
 - Patient is at least 9 years of age and older; **and**
 - Patient has relatively preserved kidney function (e.g., eGFR ≥ 30 mL/min/1.73 m²); **and**
 - Patient is not receiving Rivfloza in combination with Oxlumo (lumasiran); **and**
 - Prescribed by, or in consultation with, a specialist (e.g., geneticist, nephrologist, urologist) with expertise in the treatment of PH1; **and**
 - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
 - Initial authorization will be for no more than 12 months
- For **continuation of therapy**, all of the following:
 - Submission of medical records (e.g., chart notes, laboratory values) documenting a positive clinical response to therapy from pre-treatment baseline (e.g., decreased urinary oxalate concentrations, decreased urinary oxalate:creatinine ratio, decreased plasma oxalate concentrations); **and**
 - Patient has not received a liver transplant; **and**

- Patient has relatively preserved kidney function (e.g., eGFR \geq 30 mL/min/1.73 m²); **and**
- Patient is not receiving Rivfloza in combination with Oxlumio (lumasiran); **and**
- Prescribed by, or in consultation with, a specialist (e.g., geneticist, nephrologist, urologist) with expertise in the treatment of PH1; **and**
- Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
- Reauthorization will be for no more than 12 months

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

| HCPCS Code | Description |
|------------|--------------------|
| J3490 | Unclassified drugs |

| Diagnosis Code | Description |
|----------------|-----------------------|
| E72.53 | Primary hyperoxaluria |

Background

Primary hyperoxaluria (PH) is a rare inborn error of glyoxylate metabolism characterized by the overproduction of oxalate, which is deposited as calcium oxalate in various organs. In particular, the kidney is a prime target for oxalate deposition, as excessive urinary excretion of oxalate may lead to end-stage renal disease (ESRD). PH is primarily caused by autosomal recessive enzymatic defects in pathways of glyoxylate metabolism that result in enhanced oxalate production. PH type 1 (approximately 80 percent of cases) is due to mutations of hepatic peroxisomal enzyme alanine: glyoxylate aminotransferase (AGT). Liver transplantation is the only curative intervention for PH type 1 as it corrects the underlying enzymatic defect due to mutations of the AGXT gene.

Nedosiran reduces levels of hepatic lactate dehydrogenase (LDH) via the degradation of LDHA messenger ribonucleic acid (mRNA) in hepatocytes through RNA interference. The reduction of hepatic LDH by nedosiran reduces the production of oxalate by the liver, thereby reducing subsequent oxalate burden.

Clinical Evidence

Nedosiran

The efficacy of nedosiran was established in a randomized, double-blind trial (PHOX2) comparing nedosiran and placebo in patients aged 6 years or older with PH1 or PH2 and an eGFR \geq 30 mL/min/1.73 m² (NCT03847909). Too few PH2 patients were enrolled to evaluate efficacy in the PH2 population. Therefore, nedosiran is only indicated for patients with PH1. Patients received monthly doses of nedosiran (n = 23) or placebo (n = 12). The nedosiran dose for patients at least 12 years of age weighing at least 50 kg was 160 mg, for patients at least 12 years of age weighing less than 50 kg was 128 mg, and for children 6 to 11 years of age was 3.3 mg/kg (to a maximum of 128 mg). The median age was 20 years (range 9 - 46 years), 51% were female, 71% were White, 17% were Asian, 83% had PH1, and 17% had PH2. At baseline, mean 24-hour urinary oxalate excretion, normalized by 1.73 m² BSA in patients less than 18 years of age, was 1547 μ mol/24-hour. Mean plasma oxalate was 8.2 μ mol/L, 43% of patients had an eGFR \geq 90 mL/min/1.73 m², 34% had an eGFR 60 to < 90 mL/min/1.73 m², 23% had an eGFR 30 to < 60 mL/min/1.73 m², and 60% were taking pyridoxine. The primary efficacy endpoint was the area under the curve, from Days 90 to 180, of the percent change from baseline in 24-hour urinary oxalate excretion (AUC24-hour Uox). The least-squares (LS) mean AUC24-hour Uox was -3486 (95% CI: -5025, -1947) in the nedosiran group compared to 1490 (95% CI: 781, 3761) in the placebo group, for a between group difference of 4976 (95% CI: 2803, 7149; p < 18 years of age) averaged over Days 90, 120, 150 and 180, was -37% (95% CI: -53%, -21%) in the nedosiran group and 12% (95% CI: -12%, 36%) in the placebo group, for a between group difference of 49% (95% CI: 26%, 72%). Among patients with PH1, the between group difference was 56% (95% CI: 33%, 80%).

After 6 months of treatment, patients could enroll in an ongoing single-arm extension study, PHYOX3, in which all patients were treated with nedosiran. The reduction in urinary oxalate was maintained in the 13 patients with PH1 who received an additional 6 months of treatment in PHYOX3.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Rivfloza (nedosiran) is an LDHA-directed small interfering RNA (siRNA) indicated to lower urinary oxalate levels in children 9 years of age and older and adults with primary hyperoxaluria type 1 (PH1) and relatively preserved kidney function, e.g., eGFR \geq 30 mL/min/1.73 m².

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; 27:1729.
2. Hoppe B, Beck BB, Milliner DS. The primary hyperoxalurias. *Kidney Int* 2009; 75:1264.
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4. A Phase 1/2 Trial of Lumasiran (ALN-GO1), An Investigational RNA Interference (RNAi) Therapeutic, For Primary Hyperoxaluria Type 1. ESPN Annual Meeting. Antalya, Turkey. 4 October 2018.
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9. 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. doi:10.1016/j.kint.2022.07.025.
10. Long term extension study in patients with primary hyperoxaluria (PHYOX3). ClinicalTrials.gov website Accessed March 6, 2024.

Policy History/Revision Information

| Date | Summary of Changes |
|------------|--|
| 12/01/2024 | <p>Title Change</p> <ul style="list-style-type: none">Previously titled <i>Oxlumo® (Lumasiran) and Rivfloza™ (Nedosiran) (for Indiana Only)</i> <p>Coverage Rationale</p> <ul style="list-style-type: none">Removed coverage guidelines addressing Oxlumo® (lumasiran) <p>Applicable Codes</p> <ul style="list-style-type: none">Removed HCPCS code J0224 <p>Supporting Information</p> <ul style="list-style-type: none">Updated <i>Background, Clinical Evidence, FDA, and References</i> sections to reflect the most current informationArchived previous policy version CSIND0102.06 |

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state or contractual requirements for benefit plan coverage may differ from the standard benefit plan.

In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the InterQual[®] criteria, to assist us in administering health benefits. The UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.