Original Effective Date: 06/27/2024
Current Effective Date: 10/09/2025
Last P&T Approval/Version: 07/30/2025
Next Review Due By: 07/2026
Policy Number: C27705-A

Rivfloza (nedosiran)

PRODUCTS AFFECTED

Rivfloza (nedosiran)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Primary hyperoxaluria type 1 (PH1)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. PRIMARY HYPEROXALURIA TYPE 1 (PH1):
   1. Documented diagnosis of primary hyperoxaluria type 1
      NOTE: Due to Rivfloza mechanism of action, treatment for all subtypes may be promising but only

PH1 was demonstrated to be effective in the clinical trial
AND

2. Documentation diagnosis confirmed by alanine-glyoxylate aminotransferase (AGXT) gene mutation OR liver biopsy demonstrating significantly decreased or absent alanine: glyoxylate aminotransferase (AGT) enzyme activity [DOCUMENTATION REQUIRED]
   AND
3. The member has made efforts to increase fluid intake to at least 3 L/1.73 m2 per day
   AND
4. Documentation of concurrent use of pyridoxine or trial and failure of or serious side effects to pyridoxine for at least 3 months with no significant improvement observed (e.g., <30% reduction in urine oxalate concentration after at least 3 months of therapy.)
   AND
5. The member does not require peritoneal dialysis and the member has not had previous kidney or liver transplant
   AND
6. Laboratory documentation of member's baseline urinary oxalate level [DOCUMENTATION REQUIRE]
   OR
   IF REDUCED RENAL FUNCTION: Laboratory documentation of member's baseline plasma oxalate level [DOCUMENTATION REQUIRED]

CONTINUATION OF THERAPY:

A. PRIMARY HYPEROXALURIA TYPE 1 (PH1):
   1. Prescriber attests to or clinical review has found no evidence of disease progression or unacceptable toxicity
      AND
   2. Documentation of laboratory improvement or stabilization in urinary oxalate excretion or plasma oxalate from baseline. (Consideration for improvement as reaching near normal [< 1mmol/1.73m^2 per day] urinary oxalate excretion. Consideration for improvement is decreasing plasma oxalate level.) [DOCUMENTATION REQUIRED]
      AND
   3. The member does not require peritoneal dialysis and the member has not had previous kidney or liver transplant

DURATION OF APPROVAL:

Initial authorization: 12 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with a nephrologist, urologist or geneticist [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

2 years of age and older

QUANTITY:

Age	Body Weight	Dosing Regimen
Adults and adolescents 12 years and older	Greater than or equal to 50 kg	160 mg once monthly
	Less than 50 kg	128 mg once monthly
Children 2 to 11 years	Greater than or equal to 50 kg	160 mg once monthly
	39 to less than 50 kg	128 mg once monthly

	Less than 39 kg	3.3 mg/kg once monthly, not to exceed 128 mg (Vial, dose volume rounded to nearest 0.1 mL)

PLACE OF ADMINISTRATION:
The recommendation is that injectable medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Subcutaneous

DRUG CLASS:
Small Interfering Ribonucleic Acid Agents (siRNA)

FDA-APPROVED USES:
Indicated to lower urinary oxalate levels in children 2 years of age and older and adults with primary hyperoxaluria type 1 (PH1) and relatively preserved kidney function, e.g., eGFR ≥ 30 mL/min/1.73 m2

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Rivfloza (nedosiran) is the second agent approved by the Food and Drug Administration (FDA) for the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary oxalate levels in children 9 years of age and older and adults.

Primary hyperoxaluria is a rare inherited error of glyoxylate metabolism characterized by an excess production of oxalate. The excess oxalate is excreted by the kidneys, typically at a rate greater than 1 mmol/1.73 m2 per day (normal is less than 0.5 mmol/1.73 m2 per day). Increased urinary excretion of oxalate leads to urolithiasis and nephrocalcinosis. Progressive disease can result in end-stage kidney disease and systemic oxalate deposition.

Primary hyperoxaluria (PH) is divided into three primary types, each caused by a mutation in a gene that encodes an enzyme that plays a role in glyoxylate metabolism. PH1 is the most common type, accounting for approximately 80% of PH cases. PH1 is caused by mutation in the AGXT gene which leads to decreased activity of the hepatic alanine: glyoxylate aminotransferase (AGT) enzyme. PH2 accounts for 10% of cases and is caused by mutation in the GRHPR gene, leading to decreased activity of the glyoxylate reductase/hydroxypyruvate reductase (GRHPR) enzyme. PH3 accounts for 5% of cases and is caused by mutation in the HOGA1 gene that encodes the mitochondrial 4- hydroxy-2-oxoglutarate aldolase enzyme. In individuals with increased urinary oxalate excretion, diagnosis is confirmed by genetic testing or liver biopsy showing decreased or absent enzyme activity.

Conservative management of PH1 should include high fluid intake (greater than 3 liters/1.73 m2 per day) to reduce oxalate deposition in the kidneys. Neutral phosphate (orthophosphate), potassium citrate-citric acid and/or magnesium oxide can also be beneficial to prevent urinary oxalate precipitation. Pyridoxine is

a coenzyme of AGT that promotes the conversion of glyoxylate to glycine instead of oxalate. Up to 30% of individuals with PH1 experience a significant reduction in hyperoxaluria in response to pyridoxine therapy. A three to six-month trial of pyridoxine at a dose between 5 and 20 mg/kg per day is prudent in all individuals with PH1.
Rivfloza is a lactate dehydrogenase A (LDHA)- directed ribonucleic acid interference (RNAi) which is designed to inhibit the expression of hepatic lactate dehydrogenase (LDH). This enzyme is response for the terminal step of oxalate synthesis. The reduction in LDH by Rifvfloza reduces the production of oxalate by the liver. This thereby reduces the subsequent oxalate burden. Although reducing LDH is a promising treatment strategy for all subtypes of PH, Rivfloza is only expected to be effective in PH1. There were also too few patients enrolled in the clinical trial to evaluate the efficacy in the PH2 population.

The clinical efficacy of Rivfloza was supported by the PHYOX2 clinical trial (NCT03847909) as well as interim data from the ongoing PHYOX3 extension study (NCT04042402). PHYOX2 was a randomized, double blind, placebo-controlled trial in 35 individuals 6 years of age and older with PH1 or PH2 and an estimated glomerular filtration rate (eGFR) ≥30 mL/min/1.73 m2. Individuals with a history of renal or liver transplant, currently on dialysis or used an RNAi in the last 6 months were excluded. Patients were randomized 2:1 to receive Rivfloza (n=23) or placebo (n=12). The Rivfloza dose for patients ≥12 years of age weighing ≥50 kg was 160 mg, for patients ≥12 years of age weighing <50kg was 128mg, and for children 6 to 11 years of age was 3.3 mg/kg. The primary endpoint was percent change from baseline in 24-hour urinary oxalate (UOx) excretion. The LS mean percent change from baseline in 24-hour UOx, averaged over Days 90,120,150, and 180, was -37% in the Rivfloza group (95% CI: −53%, −21%) and 12% in the placebo group (95% CI: −12%, 36%).

After 6 months of treatment in the PHYOX2, participants were encouraged to enroll in the single-arm study, PHYOX3 (NCT04042402). This trial is ongoing to access the long-term safety and efficacy of Rivfloza. Interim results showed that the reduction in 24-hour UOx was maintained with an additional 6 months of treatment. It also showed an acceptable safety profile. The most reported AEs were injection-site reactions. These results, along with previous reports provide evidence supporting the effectiveness and safety of Rivfloza.

The dosing schedule is based on age and actual body weight and is intended for subcutaneous administration by the patient, caregiver, or health care professional.

Currently, there is one other FDA-approved treatments for PH1, Oxlumo (lumasiran) which is considered first line. Oxlumo treats PH1 by decreasing levels of the glycolate oxidase (GO) enzyme in the liver, thereby reducing a substrate necessary for oxalate production. The dosing schedule is based on actual body weight and includes three monthly loading doses followed by maintenance doses either monthly or every 3 months. It is intended for administration by a healthcare professional. Conservative management includes increasing fluid intake to 3 L/m2 BSA per day to create a high urinary output following diagnosis; this is the most effective therapy to decrease tubular fluid oxalate concentration and intratubular oxalate deposition. In addition, pyridoxine should be tried for at least 3 months in all patients with PH1, as those who respond to therapy see a significant reduction in urinary oxalate excretion that is maintained for years.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Rivfloza (nedosiran) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Rivfloza (nedosiran) include: No labeled contraindications.

OTHER SPECIAL CONSIDERATIONS:
Rivfloza is intended for subcutaneous administration by a healthcare professional, caregiver, or patient 12 years of age and older. If a planned dose is missed, administer Rivfloza as soon as possible. If the planned dose is missed by more than 7 days, administer Rivfloza as soon as possible and resume monthly dosing from the most recently administered dose.

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Rivfloza SOLN 80MG/0.5ML single-dose vial
Rivfloza SOSY 128MG/0.8ML single-dose pre-filled syringe
Rivfloza SOSY 160MG/ML single-dose pre-filled syringe

REFERENCES

1. Rivfloza (nedosiran) injection, for subcutaneous use [prescribing information]. Cambridge, MA; Novo Nordisk Inc; March 2025.
2. Syed YY. Nedosiran: First Approval. *Drugs*. 2023;83(18):1729-1733. doi:https://doi.org/10.1007/s40265-023-01976-4
3. 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
4. Nesbitt H. American Society of Nephrology | Kidney Week - Abstract Details (2020). www.asn-online.org. https://www.asn-online.org/education/kidneyweek/2020/program-abstract.aspx?controlId=3441260
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6. National Institutes of Health. In NIH trial, Long Term Extension Study in Patients with Primary Hyperoxaluria (PHYOX3, NTC04042402).
7. Oxlumo (lumasiran) injection, for subcutaneous use [prescribing information]. Cambridge, MA: Alnylam Pharmaceuticals; April 2025.

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Duration of Approval Age Restrictions Quantity References	Q3 2025

REVISION- Notable revisions: Required Medical Information Drug Class	Q3 2024
NEW CRITERIA CREATION	Q2 2024