Clinical Policy: Nedosiran (Rivfloza)

Reference Number: CP.PHAR.619
Effective Date: 09.29.23
Last Review Date: 02.26
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Nedosiran (Rivfloza®) is an *LDHA*-directed small interfering RNA.

FDA Approved Indication(s)

Rivfloza is indicated to lower urinary oxalate (UOx) 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 m^2.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Rivfloza is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Primary Hyperoxaluria Type 1 (must meet all)**:**

1. Diagnosis of PH1 confirmed by one of the following (a or b):
   a. Genetic testing confirming presence of mutations in the *AGXT* gene;
   b. Liver biopsy confirming AGT enzyme deficiency;
2. Prescribed by or in consultation with an endocrinologist, hepatologist, nephrologist, urologist, or medical geneticist;
3. Age ≥ 2 years;
4. Documentation of estimated glomerular filtration rate (eGFR) ≥ 30 mL/min/1.73 m^2;
5. Documentation of one of the following (a or b):
   a. UOx excretion > 0.70 mmol/1.73 m^2/24 h, confirmed on repeat testing;
   b. Spot urinary oxalate-to-creatinine (UOx:Cr) molar ratio greater than normal for age *(see Appendix D for reference ranges)*, confirmed on repeat testing;
6. Failure to achieve normalization of UOx excretion levels after at least three months of pyridoxine (vitamin B6) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   **Normal UOx excretion is < 0.50 mmol (< 45 mg)/1.73 m^2/day, or see Appendix D for reference ranges for age-specific spot UOx:Cr molar ratios.*
7. Member has not had a liver transplant;
8. Rivfloza is not prescribed concurrently with Oxlumo®;
9. Documentation of member's current body weight (in kg);
10. Both of the following (a and b):
    a. Request must be for a prefilled syringe unless the monthly dose is < 128 mg;

b. Dose does not exceed any of the following based on age and/or body weight (i, ii, or iii):
   i. Weight ≥ 50 kg, both of the following (1 and 2):
      1) 160 mg per month;
      2) 1 prefilled syringe per month;
   ii. Age ≥ 12 years and < 50 kg, both of the following (1 and 2):
      1) 128 mg per month;
      2) 1 prefilled syringe per month;
   iii. Age 2-11 years and < 50 kg, one of the following (1 or 2):
      1) For < 39 kg: 3.3 mg/kg;
      2) For ≥ 39 kg, both of the following (a and b):
         a) 128 mg per month;
         b) 1 prefilled syringe per month.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Primary Hyperoxaluria Type 1 (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
2. Member is responding positively to therapy as evidenced by one of the following (a or b):
   a. Decrease from baseline in UOx excretion of > 30%;

b. Improvement in PH1 symptoms (e.g., nephrolithiasis, nephrocalcinosis, kidney function, ischemic skin ulcers, metabolic bone disease, refractory anemia, cardiomyopathy, abnormalities in cardiac conduction) and one of the following (i or ii):
   i. Decrease from baseline in UOx excretion;
   ii. Improvement in spot UOx:Cr molar ratio;

3. Member has not had a liver transplant;
4. Rivfloza is not prescribed concurrently with Oxlumo;
5. Documentation of member's current body weight (in kg);
6. Both of the following (a and b):
   a. Request must be for a prefilled syringe unless the monthly dose is < 128 mg;
   b. If request is for a dose increase, new dose does not exceed any of the following based on age and/or body weight (i, ii, or iii):
      i. Weight ≥ 50 kg, both of the following (1 and 2):
         1) 160 mg per month;
         2) 1 prefilled syringe per month;
      ii. Age ≥ 12 years and < 50 kg, both of the following (1 and 2):
         1) 128 mg per month;
         2) 1 prefilled syringe per month;
      iii. Age 2-11 years and < 50 kg, one of the following (1 or 2):
         1) For < 39 kg: 3.3 mg/kg;
         2) For ≥ 39 kg, both of the following (a and b):
            a) 128 mg per month;
            b) 1 prefilled syringe per month.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AGT: alanine glyoxylate aminotransferase
FDA: Food and Drug Administration
LDHA: lactate dehydrogenase A
PH1: primary hyperoxaluria type 1
UOx: urinary oxalate
UOx:Cr: urinary oxalate-to-creatinine

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
pyridoxine	5-20 mg/kg PO QD	20 mg/kg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: Spot UOx/Cr Molar Ratio Reference Ranges in Spot Urine Samples

Age	Normal Values
0-6 months	< 325-360 mmol/mol (< 253-282 mg/g)
7-24 months	< 132-174 mmol/mol (< 103-136 mg/g)
2-5 years	< 98-101 mmol/mol (< 76-79 mg/g)
5-14 years	< 70-82 mmol/mol (< 55-64 mg/g)
> 16 years	< 40 mmol/mol (< 32 mg/g)

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
PH1	*Adults and adolescents ≥ 12 years of age* • Body weight ≥ 50 kg: 160 mg SC once monthly • Body weight < 50 kg: 128 mg SC once monthly *Children 2 to 11 years* • Body weight ≥ 50 kg: 160 mg SC once monthly • Body weight 39 kg to < 50 kg: 128 mg SC once monthly • Body weight < 39 kg: 3.3 mg/kg SC once monthly	See dosing regimen

VI. Product Availability

- Single-dose vial: 80 mg (0.5 mL)
- Single-dose prefilled syringes: 128 mg (0.8 mL), 160 mg (1 mL)

VII. References

1. Rivfloza Prescribing Information. Plainsboro, NJ: Novo Nordisk; March 2025. Available at: https://www.rivfloza.com. Accessed: November 6, 2025.
2. 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 Jan;103(1):207-217.Available at: https://www.kidney-international.org/article/S0085-2538(22)00631-7/fulltext. Accessed: November 6, 2025.
3. Milliner DS, Harris PC, Sas DJ, et al. Primary hyperoxaluria type 1. 2002 Jun 19 [Updated 2022 February 10]. In: Adam MP, Everman DB, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2023. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1283/pdf/Bookshelf_NBK1283.pdf. Accessed November 15, 2025.
4. Groothoff JW, Metry E, Deesker L, et al. Clinical practice recommendations for primary hyperoxaluria: an expert consensus statement from ERKNet and OxalEurope. Nature Reviews Nephrology. 2023;19:194-211.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
C9399	Unclassified drugs or biologicals
J3490	Unclassified drugs

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	02.28.23	05.23
RT4: Drug is now FDA approved – criteria updated per FDA labeling: minimum age revised from 6 to ≥ 9 years and maximum dosing updated per Prescribing Information; references reviewed and updated.	10.10.23	
2Q 2024 annual review: for Commercial line of business changed approval duration to "6 months or to the member's renewal date, whichever is longer"; added exclusion for concomitant use of Rivfloza with Oxlumo; for Continued Therapy clarified that one of the listed criteria would need to be met, to align with Oxlumo criteria; added urologists to the list of specialist prescribers; references reviewed and updated.	02.29.24	05.24

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2025 annual review: added HCPC codes [C9399, J3490], added medical geneticist to initial approval criteria; references reviewed and updated.	11.15.24	02.25
RT4: revised age and dosing criteria for updated pediatric extension to include children aged ≥ 2 years and added requirement that request must be for a prefilled syringe unless the monthly dose is < 128 mg.	04.16.25	
1Q 2026 annual review: no significant changes; extended initial approval duration from 6 to 12 months for this maintenance medication for a chronic condition; references reviewed and updated.	11.06.25	02.26

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise

professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.