Clinical Policy: Nedosiran (Rivfloza)

Reference Number: PA.CP.PHAR.619
Effective Date: 02/2024
Last Review Date: 01/2024

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 9 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 PA Health & Wellness® 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, or nephrologist;
3. Age ≥ 9 years;
4. Documentation of estimated glomerular filtration rate (eGFR) ≥ 30 mL/min/1.73 m^2;
5. Documentation of one of the following (a, b or c):
   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;
   c. For falsely low urinary oxalate measurements, may accept plasma oxalate levels;
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. Documentation of member's current body weight (in kg);
9. Dose does not exceed any of the following, based on age and/or body weight (a, b, or c):
   a. Weight ≥ 50 kg, both of the following (i and ii):
      i. 160 mg per month;
      ii. 1 prefilled syringe per month;

b. Age ≥ 12 years and < 50 kg, both of the following (i and ii):
   i. 128 mg per month;
   ii. 1 prefilled syringe per month;
c. Age 9-11 years and < 50 kg: 3.3 mg/kg, not to exceed 128 mg, per month.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in either of the following parameters (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. Documentation of member's current body weight (in kg);
5. If request is for a dose increase, new dose does not exceed any of the following, based on age and/or body weight (a, b, or c):
   a. Weight ≥ 50 kg, both of the following (i and ii):
      i. 160 mg per month;
      ii. 1 prefilled syringe per month;
   b. Age ≥ 12 years and < 50 kg, both of the following (i and ii):
      i. 128 mg per month;
      ii. 1 prefilled syringe per month;
   c. Age 9-11 years and < 50 kg: 3.3 mg/kg, not to exceed 128 mg, per month.

Approval duration: 12 months

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

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 – PA.CP.PMN.53

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 once monthly Body weight < 50 kg: 128 mg once monthly *Children 9 to 11 years* Body weight ≥ 50 kg: 160 mg once monthly Body weight < 50 kg: 3.3 mg/kg once monthly, not to exceed 128 mg, and the vial dose volume rounded to the nearest 0.1 mL	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; September 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/215842s000lbl.pdf. Accessed October 2, 2023.
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 October 2, 2023.
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 February 16, 2023.

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
J3490	Unclassified Drugs

Reviews, Revisions, and Approvals	Date
Policy created	01/2024