Rivfloza (nedosiran) Prior Authorization with Quantity Limit Program Summary

This program applies to Medicaid formularies.

The BCBS MN Step Therapy Supplement applies to this program for Medicaid.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
04-01-2024	04-01-2024

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Rivfloza™ (nedosiran) Injection for subcutaneous use	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 greater than or equal to 30 mL/min/1.73^2		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Primary Hyperoxaluria	The primary hyperoxalurias are rare autosomal recessive inborn errors of metabolism of which three have been described at the molecular level. Primary hyperoxaluria type 1 (PH1) results from mutations in the *AGXT* gene with associated dysfunction of the vitamin B6 (pyridoxine)-dependent liver-specific peroxisomal enzyme alanine:glyoxylate aminotransferase (AGT).(3) The disorder results in overproduction and excessive urinary excretion of oxalate, causing recurrent urolithiasis and nephrocalcinosis. As glomerular filtration rate declines due to progressive renal involvement, oxalate accumulates leading to systemic oxalosis.(2) Long-term consequences include cardiomyopathy, cardiac conduction disturbances, vasculopathy, heart block, treatment resistant anemia, oxalate osteopathy resulting in debilitating bone and joint pain, retinopathy and if untreated, early death.(4) The first sign or symptom is usually blood in the urine, pain, passage of a stone, or urinary tract infection. Patients with renal failure due to "infantile oxalosis" present with failure to thrive, anemia and acidosis. The majority of patients are symptomatic early in life and mostly before 10 years of age.(4) The usual biochemical indicator of PH1 is a persistently and markedly elevated urine oxalate (UOx) excretion in the absence of secondary causes of hyperoxaluria. Once a raised urinary oxalate has been identified, the diagnosis is confirmed through genetic testing for mutation in the *AGXT* gene OR liver biopsy indicating deficiency of AGT enzyme activity.(2,3,4) Urinary oxalate measurements may be falsely low in patients with kidney insufficiency and progressive disease, which is common in patients with PH1. In this setting, plasma oxalate levels may be useful to help support the diagnosis of PH1.(5) Therapy is recommended as soon as a diagnosis of PH1 has been confirmed. High fluid intake is mandatory and may require the placement of a nasogastric or gastrostomy feeding tube. Alkalization of the urine with potassium citrate is recommended to reduce urinary calcium oxalate precipitation thus decreasing stone growth or

	nephrocalcinosis.(2,3,4) It may be replaced by sodium citrate appropriate to GFR and plasma potassium.(2,4) Pyridoxine (vitamin B6) is a co-factor for AGT and the administration of pyridoxine has been associated with a decrease in urine oxalate in about 30% of PH1 patients. Guidelines recommend that all patients receive administration of pyridoxine for a test period of a minimum of 3 months.(2,3,4) For those patients who are responsive (defined as a greater than 30% decrease in urine oxalate), pyridoxine should be continued indefinitely or until liver transplantation. To date, the only curative treatment for PH1 is combined liver-kidney transplantation.(2,4)
Efficacy	PHYOX2 was a randomized, double-blind trial (NCT03847909) comparing Rivfloza and placebo in patients aged 6 years or older with PH1 or PH2 and an eGFR greater than or equal to 30 mL/min/1.73 m^2. Patients received monthly doses of Rivfloza (n=23) or placebo (n=12). In the patient population, 83% had PH1, and 17% had PH2; 60% were taking pyridoxine.(1) Additional criteria include (but are not limited to): diagnosis must be genetically confirmed, no kidney or liver transplantation (previous or planned).(6) 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 (AUC-24h-Uox). The least-squares (LS) mean AUC-24h-Uox was -3486 (95% CI: -5025, -1947) in the Rivfloza group compared to 1490 (95% CI: 781, 3761) in the placebo group, for a between group difference of 4976 (95% CI: 2803, 7149; p less than 0.0001). The LS mean percent change from baseline in 24-hour urinary oxalate excretion averaged over Days 90, 120, 150 and 180, was -37% (95% CI: -53%, -21%) in the Rivfloza group and 12% (95% CI: -12%, 36%) in the placebo group, for a between group difference of 49% (95% CI: 26%, 72%). Among patients specifically with PH1, the between group difference was 56% (95% CI: 33%, 80%). After 6 months of treatment in PHYOX2, patients could enroll in an ongoing single-arm extension study, PHYOX3 (NCT04042402), in which all patients were treated with Rivfloza. The reduction in urinary oxalate was maintained in the 13 patients with PH1 who received an additional 6 months of treatment in PHYOX3.(1) Too few PH2 patients were enrolled to evaluate efficacy in the PH2 population. Therefore, Rivfloza is only indicated for patients with PH1.(1)
Safety	Rivloza (nedosiran) has no boxed warnings or contraindications.(1)

REFERENCES

Number	Reference
1	Rivfloza prescribing information. Novo Nordisk Inc. September 2023.
2	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;27:1729-1736.
3	Hulton SA. The Primary Hyperoxalurias: A Practical Approach to Diagnosis and Treatment. Int J Surg. 2016 Dec;36(D):649-654.
4	Hoppe B, Beck BB, Milliner D. The Primary Hyperoxalurias. Kidney Int. 2009 Jun;75(12):1264-1271.
5	Niaudet P, et al. Primary Hyperoxaluria. UpToDate. Literature review current through September. Last updated August 2023.
6	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.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Rivfloza	nedosiran		M ; N ; O ; Y	Y		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Rivfloza 128 mg single-dose prefilled syringe	nedosiran		1	Syringe	30	DAYS			
Rivfloza 160 mg single-dose prefilled syringe	nedosiran		1	Syringe	30	DAYS			
Rivfloza 80 mg single-dose vial	nedosiran		2	Vials	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Rivfloza	nedosiran		Medicaid

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Rivfloza 128 mg single-dose prefilled syringe	nedosiran		Medicaid
Rivfloza 160 mg single-dose prefilled syringe	nedosiran		Medicaid
Rivfloza 80 mg single-dose vial	nedosiran		Medicaid

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has a diagnosis of primary hyperoxaluria type 1 (PH1) confirmed by ONE of the following: A. Genetic testing of the *AGXT* gene indicates a pathogenic mutation **OR** B. Liver biopsy demonstrates absent or significantly reduced alanine:glyoxylate aminotransferase (AGT) activity **AND** 2. The requested agent will be used to lower urinary oxalate levels **AND** 3. The patient has an estimated GFR (eGFR) greater than or equal to 30 mL/min/1.73^2 **AND** 4. If the patient has an FDA approved indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND**

Module	Clinical Criteria for Approval
	5. ONE of the following: A. The patient's medication history includes potassium citrate or sodium citrate **AND** ONE of the following: 1. The patient has had an inadequate response to potassium citrate or sodium citrate **OR** 2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over BOTH potassium citrate and sodium citrate **OR** B. The patient has an intolerance or hypersensitivity to potassium citrate or sodium citrate therapy **OR** C. The patient has an FDA labeled contraindication to BOTH potassium citrate AND sodium citrate **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that BOTH potassium citrate and sodium citrate cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional **AND** 6. ONE of the following: A. The patient's medication history includes pyridoxine (vitamin B6) for at least 3 months **AND** ONE of the following: 1. The patient has had an inadequate response to pyridoxine (vitamin B6) (inadequate response defined as less than or equal to 30% decrease in urine oxalate after 3 months of treatment with maximally tolerated pyridoxine) **OR** 2. The patient is responsive to pyridoxine (vitamin B6) (responsive defined as greater than 30% decrease in urine oxalate after 3 months of treatment with maximally tolerated pyridoxine) **AND** will continue treatment with pyridoxine (vitamin B6) in combination with the requested agent **OR** 3. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over pyridoxine (vitamin B6) **OR** B. The patient has an intolerance or hypersensitivity to pyridoxine (vitamin B6) therapy **OR** C. The patient has an FDA labeled contraindication to pyridoxine (vitamin B6) **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that pyridoxine (vitamin B6) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional **AND** 7. The patient has not received a kidney or liver transplant **AND** 8. The prescriber is a specialist in the area of the patient's diagnosis (e.g., gastroenterologist, nephrologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 9. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 6 months

Module	Clinical Criteria for Approval
	Renewal Evaluation **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process **AND** 2. The patient has had clinical benefit with the requested agent (e.g., decrease in urinary oxalate levels) **AND** 3. The patient has an estimated GFR (eGFR) greater than or equal to 30 mL/min/1.73^2 **AND** 4. ONE of the following: A. The patient's medication history includes pyridoxine (vitamin B6) **AND** ONE of the following: 1. The patient will continue treatment with pyridoxine (vitamin B6) in combination with the requested agent **OR** 2. The patient has had an inadequate response to pyridoxine (vitamin B6) (inadequate response defined as less than or equal to 30% decrease in urine oxalate after 3 months of treatment with maximally tolerated pyridoxine) **OR** 3. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over pyridoxine (vitamin B6) **OR** B. The patient has an intolerance or hypersensitivity to pyridoxine (vitamin B6) therapy **OR** C. The patient has an FDA labeled contraindication to pyridoxine (vitamin B6) **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that pyridoxine (vitamin B6) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional **AND** 5. The patient has not received a kidney or liver transplant **AND** 6. The prescriber is a specialist in the area of the patient's diagnosis (e.g., gastroenterologist, nephrologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 7. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Quantity limit for the Target Agent(s) will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit **Length of Approval:** 6 months (Initial); 12 months (Renewal)