09-J4000-79

Original Effective Date: 04/01/24

Reviewed: 02/14/24

Revised: 00/00/00

Subject: Nedosiran (Rivfloza) subcutaneous injection

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Dosage/ Administration	Position Statement	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		

DESCRIPTION:

Primary hyperoxaluria type 1 (PH1) is a metabolic disorder that causes the overproduction of oxalate. Calcium oxalate crystals form in the kidneys and result in recurrent nephrolithiasis, nephrocalcinosis, and progressively leads to renal dysfunction. Plasma accumulation of oxalate occurs as renal function declines and may cause damage to other organs (e.g., retina, myocardium, blood vessels, bone).

PH1 is caused by a autosomal recessive genetic mutation of the AGXT gene which results in dysfunction of the liver enzyme alanine:glyoxylate aminotransferase (AGT). The deficient AGT enzyme results in the conversion of glyoxylate to oxalate. AGT is a pyridoxal dependent enzyme and approximately 30-50% of patients may respond to pyridoxine treatment. A greater than 30% reduction in urine oxalate excretion after a minimum of 3 months of maximal pyridoxine (5 to 20 mg/kg/day) is considered a response. Other treatment options include reducing the formation of crystals in the urine through hyperhydration and urine alkalization with potassium citrate or sodium citrate. As disease progresses, dialysis may be necessary to remove excess plasma oxalate until liver transplant can occur.

Nedosiran (Rivfloza) is FDA approved for the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary oxalate levels in pediatric patients 9 years and older and adult patients with preserved renal function (e.g., eGFR ≥30 ml/min/1.73 m^2). It works in hepatocytes by interfering with lactate dehydrogenase A (LDHA) messenger ribonucleic acid (mRNA) and reduces levels of hepatic LDH. This decreases the production of oxalate by the liver.

The efficacy of nedosiran was evaluated in a randomized, double-blind, placebo controlled trial in patients ≥6 years of age with PH1 or PH2. There were not enough patients with PH2 to evaluate efficacy. There were 60% of subjects receiving pyridoxine. The primary efficacy endpoint was the area under the curve from day 90 to 180 or the percent change from baseline in 24-hour urinary oxalate excretion. There was a statistically significant reduction in 24-hour urinary oxalate excretion between

Day 90 and 180 from baseline compared with placebo [least-squares mean difference (95% CI) of 4976 (2803, 7149), p<0.0001] . The least squares mean percent change difference from baseline in 24-hour urinary oxalate excretion (corrected for BSA in patients < 18 years of age) averaged over Days 90, 120, 150, and 180 in subjects with PH1 was also improved with nedosiran as compared to placebo (-37% vs 12%). Reductions in 24-hour urinary oxalate excretion were maintained in the 13 patients with PH1 who received an additional 6 months of treatment in an extension study. The most common adverse reactions were mild injection site reactions (erythema, pain, bruising, and rash).

POSITION STATEMENT:

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of nedosiran (Rivfloza) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Member is diagnosed with primary hyperoxaluria type 1 (PH1) confirmed by **ONE** of the following – lab documentation must be provided:
    a. Presence of a pathogenic AGXT gene mutation
    b. Liver biopsy demonstrates an alanine-glyoxylate aminotransferase (AGT) enzyme deficieny
2. Member demonstrates **ONE** of the following – documentation must be provided:
    a. Elevated 24 hour urine oxalate excretion corrected for body surface area (BSA) greater than the upper limit of normal (ULN)
    b. Elevated spot urine oxalate:creatinine ratio greater than the age-specific ULN
    c. Elevated plasma oxalate concentration greater than the ULN
3. **ONE** of the following:
    a. The member had an inadequate response to pyridoxine (i.e., ≤30% decrease in urine oxalate after 3 months of treatment with maximally tolerated pyridoxine)
    b. The member has a contraindication or intolerance to pyridoxine
    c. The member will receive treatment in combination with pyridoxine
4. Member does not have primary hyperoxaluria type 2 or primary hyperoxaluria type 3
5. Member has not previously had a liver transplant
6. Nedosiran is prescribed by or in consultation with a nephrologist, urologist, hepatologist, gastroenterologist, or geneticist
7. The member does not have severe renal dysfunction (i.e., eGFR less than 30 ml/min/1.73 m^2)
8. Nedosiran will not be used in combination with lumasiran (Oxlumo)
9. The dose does not exceed weight based dosing in Table 1.

Approval duration: 6 months

Continuation of nedosiran (Rivfloza) **meets the definition of medical necessity** for the treatment of primary hyperoxaluria type 1 when **ALL** of the following criteria are met:

1. An authorization or reauthorization for nedosiran has been previously approved by Florida Blue or another health plan in the past 2 years for the treatment of primary hyperoxaluria type 1 (if another health plan, documentation of a health plan-paid claim for nedosiran during the 90 days immediately before the authorization request must be provided), **OR** the member has previously met **ALL** indication-specific criteria.
2. The member had a beneficial response to treatment (e.g., reduction of urine oxalate excretion or plasma oxalate levels from baseline) – documentation must be submitted
3. Member does not have primary hyperoxaluria type 2 or primary hyperoxaluria type 3
4. Member has not previously had a liver transplant
5. Nedosiran is prescribed by or in consultation with a nephrologist, urologist, hepatologist, gastroenterologist, or geneticist
6. The member does not have severe renal dysfunction (i.e., eGFR less than 30 ml/min/1.73 m^2)
7. Nedosiran will not be used in combination with lumasiran (Oxlumo)
8. The dose does not exceed weight based dosing in Table 1.

Approval duration: 12 months

Table 1. Dosing of Nedosiran (Rivfloza™)

Age	Body Weight	Dosing Regimen
Adults and adolescents 12 years and older	Greater than or equal to 50 kg	160 mg once monthly (pre-filled syringe, 1 mL)
	Less than 50 kg	128 mg once monthly (pre-filled syringe, 0.8 mL)
Children 9 to 11 years	Greater than or equal to 50 kg	160 mg once monthly (pre-filled syringe, 1 mL)
	Less than 50 kg	3 mg/kg once monthly, not to exceed 128 mg (Vial, dose volume rounded to the nearest 0.1 mL)

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

Nedosiran (Rivfloza) is FDA approved for the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary oxalate levels in pediatric patients 9 years and older and adult patients with preserved renal function (e.g., eGFR ≥30 ml/min/1.73 m^2)

Age	Body Weight	Dosing Regimen
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Children 9 to 11 years	Greater than or equal to 50 kg	160 mg once monthly (pre-filled syringe, 1 mL)
	Less than 50 kg	3 mg/kg once monthly, not to exceed 128 mg (Vial, dose volume rounded to the nearest 0.1 mL)

If a dose is missed, administer as soon as possible. If the planned dose is missed by more than 7 days, administer as soon as possible and resume monthly dosing from the most recently administered dose. See prescribing information for administration instructions.

PRECAUTIONS:

Boxed Warning- none

Contraindications- none

Precautions/Warnings -none

Drug Availability

- 80 mg (0.5 mL) single-dose vial
- 128 mg (0.8 mL) single-dose Pre-filled syringe
- 160 mg (1 mL) single-dose Pre-filled syringe

BILLING/CODING INFORMATION:

HCPCS Coding

J3490	Unclassified drugs

ICD-10 Diagnosis Codes That Support Medical Necessity

E72.53	Primary hyperoxaluria

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 02/14/24.

GUIDELINE UPDATE INFORMATION:

04/01/24	New Medical Coverage Guideline.