Medical Drug Clinical Criteria

Subject:	Rivfloza (nedosiran)		
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Overview

This document addresses the use of Rivfloza (nedosiran), a *LDHA*-directed small interfering RNA approved by the Food and Drug Administration (FDA) 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 (eGFR ≥ 30 mL/min/1.73 m^2). Rivfloza is administered subcutaneously once monthly by the individual, caregiver or health care professional.

Primary hyperoxaluria (PH) is divided into three 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 PH should include high fluid intake (greater than 3 liters/1.73 m^2 per day) to reduce oxalate deposition in the kidneys. Alkalinization of urine 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. 30-50% of individuals with PH1 experience a significant reduction in hyperoxaluria in response to pyridoxine therapy. A trial of pyridoxine at a dose between 5 and 20 mg/kg per day is prudent in individuals with a pyridoxine-responsive genotype of PH1.

The clinical efficacy of Rivfloza was demonstrated in PHYOX2, a randomized, double-blind, placebo-controlled trial. PHYOX2 included 35 individuals age 6 and older with PH1 or PH2 and an eGFR ≥ 30 mL/min/1.73 m^2. Individuals with a history of renal or liver transplant were excluded. The number of participants with PH2 was too low to evaluate efficacy in that population so FDA approval was limited to individuals with PH1. The primary efficacy endpoint was the area under the curve of the percent change from baseline in 24-hour urinary oxalate excretion from day 90 to 180 and was significantly greater with Rivfloza compared to placebo ($p < 0.001$).

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Rivfloza (nedosiran)

Initial requests for Rivfloza (nedosiran) may be approved if the following criteria are met:

I. Individual is 9 years of age or older; **AND**
II. Individual has a diagnosis of primary hyperoxaluria type 1 (PH1); **AND**
III. Documentation is provided that diagnosis has been verified by (Cochat 2012; Milliner 2022):

A. Genetic testing demonstrating mutation in the alanine-glyoxylate aminotransferase (AGXT) gene; **OR**
B. Liver biopsy demonstrating significantly decreased or absent alanine-glyoxylate aminotransferase (AGT) enzyme activity; **AND**

IV. Documentation is provided that individual has elevated urinary oxalate levels; **AND**
V. Individual is using in combination with pyridoxine (unless individual is a pyridoxine non-responder) (Cochat 2012; Milliner 2022).

Continuation requests for Rivfloza (nedosiran) may be approved if the following criteria are met:

I. Documentation is provided that there is a clinically significant reduction in urinary oxalate excretion with Rivfloza therapy; **AND**
II. Individual is using in combination with pyridoxine (unless individual is a pyridoxine non-responder) (Cochat 2012; Milliner 2022).

Rivfloza (nedosiran) may not be approved for the following:

I. Individual with primary hyperoxaluria type 2 or type 3; **OR**
II. Individual with a history of or planned kidney or liver transplant (Baum 2023); **OR**
III. Individual has an estimated glomerular filtration rate (eGFR) less than 30 mL/min/1.73 m^2; **OR**
IV. Use in combination with Oxlumo (lumasiran); **OR**
V. May not be approved when the above criteria are not met and for all other indications.

Approval Duration
Initial: 6 months
Continuation: 1 year

Quantity Limits

Rivfloza (nedosiran) Quantity Limit

Drug	Limit
Rivfloza (nedosiran) 80 mg vial	2 vials per month
Rivfloza (nedosiran) 128 mg prefilled syringe	1 syringe per month
Rivfloza (nedosiran) 160 mg prefilled syringe	1 syringe per month

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J3490	Unclassified drugs (when specified as [Rivfloza] (nedosiran))

ICD-10 Diagnosis

	All diagnoses pend

Document History

New: 12/11/2023
Document History:

- 12/11/2023 – Annual Review: New clinical criteria and quantity limit for Rivfloza. Coding Reviewed: Added HCPCS J3490. All diagnoses pend.

References

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6. Milliner DS, Harris PC, Sas DJ, et al. Primary Hyperoxaluria Type 1. 2002 Jun 19 [Updated 2022 Feb 10]. In: Adam MP, Everman DB, Mirzaa GM, et al., editors. GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1283/.
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