Medical Drug Clinical Criteria

Subject:	Onpattro (patisiran)		
Document #:	CC-0082	**Publish Date**:	09/23/2024
Status:	Revised	**Last Review Date**:	08/16/2024

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Overview

This document addresses the use of Onpattro (patisiran), an RNA interference (RNAi) therapeutic agent approved by the Food and Drug Administration for the treatment of polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis in adults. hATTR amyloidosis was formerly known as familial amyloid polyneuropathy (FAP).

Hereditary transthyretin (hATTR) amyloidosis is a multisystemic, progressive, life-threatening disease characterized by extracellular deposition of amyloid fibrils composed of misfolded transthyretin (TTR), a plasma transport protein produced predominantly by the liver. Amyloid fibrils accumulate in various organs and tissues including the heart, kidney, gastrointestinal tract, and peripheral nerves, resulting in clinical manifestations such as polyneuropathy and cardiomyopathy. Potential symptoms associated with hATTR amyloidosis include but are not limited to muscle weakness, difficulty ambulating, impaired balance, orthostatic hypotension, disturbances in GI mobility, heart failure, arrhythmias, and sudden death due to severe conduction disorders.

Due to the constellation of symptoms and multisystemic nature of the disease, various assessments need to be utilized in an effort to quantify the overall disease burden for each individual with hATTR amyloidosis. Examples of clinical tests include the Neuropathy Impairment Score (NIS) and Polyneuropathy Disability (PND) Score. Clinical trials evaluated the use of Onpattro in individuals with hATTR amyloidosis and mild to moderate polyneuropathy. An example of mild to moderate polyneuropathy status is an individual who is able to ambulate with or without the use of assistance.

The efficacy of Onpattro was demonstrated in a randomized, double-blind, placebo-controlled trial in 225 adults with hereditary transthyretin amyloidosis with polyneuropathy. Study participants had a Neuropathy Impairment Score (NIS) of 5-130 (NIS scale ranges from 0-244), a polyneuropathy disability score of IIIb or lower and a TTR mutation confirmed by genotyping. Key exclusion criteria were previous liver transplant, New York Heart Association (NYHA) class III or IV heart failure, severe renal impairment or end-stage renal disease, moderate or severe hepatic impairment and other causes of polyneuropathy unrelated to hATTR amyloidosis. The primary efficacy assessment favored Onpattro over placebo. The difference in least-squares mean change from baseline to 18 months between groups was -34.0 points (95% CI -39.9 to -28.1) for the standardized modified Neuropathy Impairment Score+7 (mNIS+7) composite score.

The recommended Onpattro dosage for individuals weighing less than 100 kg is 0.3 mg/kg every 3 weeks. For individuals weighing 100 kg or more, the recommended Onpattro dosage is 30 mg every 3 weeks. Treatment with Onpattro leads to a decrease in serum vitamin A levels. Individuals should be advised to take vitamin A supplementation at the recommended daily allowance while receiving Onpattro therapy.

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.

Onpattro (patisiran)

Initial requests for Onpattro (patisiran) may be approved if the following criteria are met:

I. Individual has a diagnosis of hereditary transthyretin (hATTR) amyloidosis or familial amyloid polyneuropathy (FAP); **AND**
II. Documentation is provided that individual has a TTR mutation verified by genotyping (Adams, 2018); **AND**
III. Documentation is provided that individual has associated mild to moderate polyneuropathy (Adams, 2018).

Continuation requests for Onpattro (patisiran) may be approved if the following criterion is met:

I. Documentation is provided to show clinically significant improvement or stabilization in clinical signs and symptoms of disease (including but not limited to improved ambulation, improvement in neurologic symptom burden, improvement in activities of daily living).

Requests for Onpattro (patisiran) may not be approved for the following:

I. Individual has a history of liver transplantation (Adams 2018); **OR**
II. Individual has severe renal impairment or end-stage renal disease; **OR**
III. Individual has moderate or severe hepatic impairment; **OR**
IV. Individual has New York Heart Association (NYHA) class III or IV heart failure (Adams, 2018); **OR**
V. Individual has sensorimotor or autonomic neuropathy not related to hATTR amyloidosis (monoclonal gammopathy, autoimmune disease, etc.) (Adams, 2017); **OR**
VI. Individual is using in combination with Amvuttra, Tegsedi, Vyndaqel, Vyndamax, or Wainua; **OR**
VII. May not be approved when the above criteria are not met and for all other indications.

Quantity Limits

Onpattro (patisiran) Quantity Limit

Drug	Limit
Onpattro (patisiran) 10 mg/5 mL vial	0.3 mg/kg [max dose 30 mg (3 vials)] every 3 weeks

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

J0222	Injection, Patisiran, 0.1 mg [Onpattro]

ICD-10 Diagnosis

E85.1-E85.9	Neuropathic heredofamilial amyloidosis
G62.9	Polyneuropathy unspecified

Document History

Revised: 8/16/2024
Document History:

- 8/16/2024 – Annual Review: Add Wainua to may not be used in combination criteria. Coding Reviewed: No changes.
- 8/18/2023 – Annual Review: Wording and formatting changes. Coding Reviewed: No changes.
- 8/19/2022 – Annual Review: Add may not approve criteria for combination use with Amvuttra. Wording and formatting changes. Coding reviewed: No changes.
- 08/20/2021 – Annual Review: No changes. Coding reviewed: No changes.
- 08/01/2021 – Administrative update to add documentation.
- 08/21/2020 – Annual Review: Add continuation criteria to Onpattro clinical criteria. Add Onpattro quantity limit. Coding Reviewed: No changes.
- 08/16/2019 – Annual Review: Add may not approve criteria for combination use with other agents for amyloidosis. Wording and formatting changes. Coding Reviewed: Added J0222 for Onpattro Effective

(10/1/19), Delete HCPCS J3490, C9036 (Effective 10/1/19) Added ICD-10 codes G62.9 and extended code range E85.1-E85.9 to include TTR mutation.

- 11/21/2018 – Deleted HCPCS codes C9399. Added HCPCS codes: C9036.
- 11/8/2018 – Added ICD-10 E85.1.
- 11/2/2018 – Added HCPCS codes: C9399 and J3490.
- 08/17/2018 – Annual Review: Add new clinical criteria for Onpattro.

References

1. Adams D, Gonzalez-Duarte A, O'Riordan WD, et al. Patisiran, an RNAi therapeutic, for hereditary transthyretin amyloidosis. *N Engl J Med*. 2018;379(1):11-21.
2. Adams D, Suhr OB, Dyck PJ, et al. Trial design and rationale for APOLLO, a Phase 3, placebo-controlled study of patisiran in patients with hereditary ATTR amyloidosis with polyneuropathy. *BMC Neurol*. 2017;17(1):181.
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4. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: July 3, 2024.
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7. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

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