Medical Policy

Utilization Management and Clinical Medical Policy

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
patisiran (Onpattro®)	MP-RX-FP-194-26	☒ MMM MA ☒ MMM MultiHealth	10/21/2026	10/21/2026
			Last Review Date: 10/21/2026	Frequently Revision: Annual

Service Category:

- ☐ Anesthesia
- ☐ Surgery
- ☐ Radiology Procedures
- ☐ Pathology and Laboratory Procedures
- ☐ Medicine Services and Procedures
- ☐ Evaluation and Management Services
- ☐ DME/Prosthetics or Supplies
- ☒ Other: Part B Drugs

Service Description:

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).

Background Information:

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.

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Approved Indications

A. For the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

Other Uses

A. None.

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Medical Necessity Guidelines:

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.

patisiran (Onpattro®)

A. Criteria For Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

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).

B. Criteria For Continuation of Therapy

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

i. Individual has a diagnosis of polyneuropathy of hereditary transthyretin (hATTR) amyloidosis; **AND**
ii. Documentation is provided that individual has a TTR mutation verified by genotyping (Adams 2018); **AND**
iii. 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).

C. Authorization Duration

i. Initial Approval Duration: Up to 6 months
ii. Reauthorization Approval Duration: Up to 6 months

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

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 New York Heart Association (NYHA) class III or IV heart failure (Adams, 2018); **OR**

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iii. Individual has sensorimotor or autonomic neuropathy not related to hATTR amyloidosis (monoclonal gammopathy, autoimmune disease, etc.) (Adams, 2017); **OR**

iv. Individual is using in combination with Amvuttra, Attruby,Tegsedi, Vyndaqel, Vyndamax, or Wainua; **OR**

v. May not be approved when the above criteria are not met and for all other indications.

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Limits or Restrictions:

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Drug	Recommended Dosing Schedule
Onpattro (patisiran) inj. 10 mg/5 mL single dose vial	• Patients weighing < 100 kg: 0.3 mg/kg IV every 3 weeks • Patients weighing 100 kg or more: 30 mg (3 vials) IV every 3 weeks
Exceptions	
• Dosing is based on actual body weight.	

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Codes Information:

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

ICD-10 Diagnostic Codes:

Codes	Description
E85.1	Neuropathic heredofamilial amyloidosis [transthyretin-related (ATTR) familial amyloid polyneuropathy]

HCPCS Codes:

Codes	Description
J0222	

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Reference Information:

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.
3. Ando Y, Coelho T, Berk JL, et. al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. Orphanet J Rare Dis. 2013;8(31).
4. Alnylam Pharmaceuticals, Inc. Onpattro® (patisiran) prescribing information. Revised September 2025. Available at: https://www.alnylam.com/sites/default/files/pdfs/ONPATTRO-Prescribing-Information.pdf. Accessed August 25, 2026.
5. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: June 21, 2025.
6. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
7. Gertz MA, Benson MD, Dyck PJ, et. al. Diagnosis, Prognosis, and Therapy of Transthyretin Amyloidosis. J Am Coll Cardiol. 2015;66(21):2451-2466.
8. 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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Policy History:

Type of Review	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Policy Inception	Elevance Health's Medical Policy adoption.	**10/15/2026**	**10/21/2026**