Clinical Policy: Patisiran (Onpattro)

Reference Number: CP.PHAR.395
Effective Date: 09.11.18
Last Review Date: 05.26
Line of Business: Commercial, Medicaid, HIM/ICHRA

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Patisiran (Onpattro®) is a transthyretin (TTR)-directed small interfering ribonucleic acid.

FDA Approved Indication(s)

Onpattro is indicated for the treatment of the polyneuropathy of hereditary TTR-mediated amyloidosis in adults.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Onpattro is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Hereditary Transthyretin-Mediated Amyloidosis (must meet all)**:**

1. Diagnosis of hereditary TTR-mediated amyloidosis with polyneuropathy;
2. Documentation confirms presence of a TTR mutation;
3. One of the following (a or b):
   a. Biopsy is positive for amyloid deposits;
   b. Medical justification is provided as to why treatment should be initiated despite a negative biopsy or no biopsy;
4. Prescribed by or in consultation with a neurologist;
5. Age ≥ 18 years;
6. Member has not had a prior liver transplant;
7. Onpattro is not prescribed concurrently with Amvuttra or Wainua;
8. Dose does not exceed the following (based on actual body weight):
   a. Weight < 100 kg: 0.3 mg/kg once every 3 weeks;
   b. Weight ≥ 100 kg: 30 mg once every 3 weeks.

Approval duration:
Medicaid/HIM/ICHRA – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):

a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Hereditary Transthyretin-Mediated Amyloidosis (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
2. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in any of the following parameters: measures of polyneuropathy (e.g., motor strength, sensation, and reflexes), quality of life, motor function, walking ability (e.g., as measured by timed 10-m walk test), and nutritional status (e.g., as evaluated by modified mass index)];
3. Member has not had a prior liver transplant;
4. Onpattro is not prescribed concurrently with Amvuttra or Wainua;
5. If request is for a dose increase, new dose does not exceed the following (based on actual body weight):
   a. Weight < 100 kg: 0.3 mg/kg once every 3 weeks;
   b. Weight ≥ 100 kg: 30 mg once every 3 weeks.

Approval duration:
Medicaid/HIM/ICHRA – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
TTR: transthyretin

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: General Information

- To confirm amyloidosis, the demonstration of amyloid deposits via tissue biopsy is essential. Deposition of amyloid in the tissue can be demonstrated by Congo red staining of biopsy specimens. With Congo red staining, amyloid deposits show a characteristic green birefringence under polarized light; however, negative biopsy results should not be interpreted as excluding the disease.
- DNA sequencing is usually required for genetic confirmation. Current techniques for performing sequence analysis of TTR, the only gene known to be associated with TTR amyloidosis, detect > 99% of disease-causing mutations.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Hereditary TTR-mediated amyloidosis-associated polyneuropathy	• Adults weighing < 100 kg: 0.3 mg/kg IV every 3 weeks • Adults weighing ≥ 100 kg: 30 mg IV every 3 weeks • Premedicate with a corticosteroid, acetaminophen, and antihistamines to reduce the risk of infusion-related reactions.	See dosing regimen

Indication	Dosing Regimen	Maximum Dose
	• Onpattro should be administered by a healthcare professional.	

VI. Product Availability

Lipid complex injection (single-dose vial): 10 mg/5 mL (2 mg/mL)

VII. References

1. Onpattro Prescribing Information. Cambridge, MA: Alnylam Pharmaceuticals, Inc.; September 2025. Available at: https://www.alnylam.com/sites/default/files/pdfs/ONPATTRO-Prescribing-Information.pdf. Accessed January 14, 2026.
2. Ando Y, Coelho T, Berk JL, et al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. Orphanet J Rare Dis. 2013 Feb 20;8:31.
3. Adams D, Gonzalez-Duarte A, O'Riordan WD, et al. Patisiran, an RNAi Therapeutic, for Hereditary Transthyretin Amyloidosis. N Engl J Med. 2018 Jul 5;379(1):11-21.
4. Magrinelli F, Fabrizi GM, Santoro L, et al. Pharmacological treatment for familial amyloid polyneuropathy. Cochrane Database Syst Rev. 2020;4(4):CD012395.
5. Alcantara M, Mezei MM, Baker SK, et al. Canadian guidelines for hereditary transthyretin amyloidosis polyneuropathy management. Can J Neurol Sci. 2022;49(1):7-18.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J0222	Injection, patisiran, 0.1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2022 annual review: added criterion for no prior treatment with Amvuttra or Tegsedi in initial approval criteria due to lack of supportive evidence; updated concurrent use exclusion with recently approved TTR-directed small interfering ribonucleic acid Amvuttra for both initial and continued approval criteria; included criterion for no prior liver transplant for continued approval criteria (already exists in initial approval criteria); clarified approval duration for commercial line of business injectable drug is 6 months or to the member's renewal date, whichever is longer; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	08.01.22	11.22
4Q 2023 annual review: no significant changes; references reviewed and updated.	07.10.23	11.23

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2024 annual review: added Wainua to list of drugs that should not have been previously received or prescribed concurrently; references reviewed and updated.	01.09.24	05.24
2Q 2025 annual review: removed criteria "member has not received prior treatment with Amvuttra, Tegsedi, or Wainua" per competitor analysis and to allow alternative therapy as a result of Tegsedi market withdrawal; references reviewed and updated.	01.17.25	05.25
2Q 2026 annual review: no significant changes; removed Tegsedi from criteria as agent is discontinued; for Medicaid/HIM revised initial approval duration from 6 to 12 months; references reviewed and updated. Added ICHRA line of business.	03.26.26	05.26

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.