Corporate Medical Policy: Patisiran (Onpattro®) **"Notification"** **POLICY EFFECTIVE OCTOBER 1, 2025**

Restricted Product(s):

- patisiran (Onpattro®) intravenous infusion for administration by a healthcare professional

FDA Approved Use:

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

Criteria for Medical Necessity:

The restricted product(s) may be considered medically necessary when the following criteria are met:

Initial Criteria for Approval:

1. The patient is 18 years of age or older; **AND**
2. The patient has a diagnosis of **polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR-PN) [medical record documentation required]**; **AND**
3. The diagnosis has been confirmed by both of the following:
    a. Genetic testing demonstrating *TTR* gene mutation **[medical record documentation required]**; **AND**
    b. Presence of clinical signs and symptoms of hATTR **[medical record documentation required]**; **AND**
4. The patient has **peripheral neuropathy** associated with hATTR with all of the following:
    a. ONE of the following:
        i. Baseline polyneuropathy disability (PND) score of IIIb or lower **[medical record documentation required]**; **OR**
        ii. Baseline Familial Amyloid Polyneuropathy (FAP) stage 1 or 2 **[medical record documentation required]**; **AND**
    b. Abnormal electrodiagnostic (nerve conduction) studies consistent with hATTR-associated polyneuropathy **[medical record documentation required]**; **AND**
    c. Other causes of peripheral neuropathy have been excluded **[medical record documentation required]**; **AND**
5. ONE of the following:
    a. The patient has tried and had an inadequate response to eplontersen (Wainua) **[medical record documentation required]**; **OR**
    b. The patient has an intolerance or hypersensitivity to eplontersen (Wainua) **[medical record documentation required]**; **OR**
    c. The patient has an FDA labeled contraindication to eplontersen (Wainua) **[medical record documentation required]**; **OR**

   d. The patient is diagnosed with hATTR with a mixed phenotype, exhibiting both polyneuropathy and cardiomyopathy **[medical record documentation required]**; **AND**
6. The patient has NOT had prior liver transplantation **[medical record documentation required]**; **AND**
7. The patient will NOT receive the requested agent in combination with any other TTR-directed therapy (e.g., acoramidis [Attruby], eplontersen [Wainua], inotersen [Tegsedi], tafamidis [Vyndamax], tafamidis meglumine [Vyndaqel], or vutrisiran [Amvuttra]) **[medical record documentation required]**; **AND**
8. The prescriber is a specialist in the area of the patient's diagnosis (e.g., geneticist, neurologist or specialist in the treatment of amyloidosis) or has consulted with a specialist in the area of the patient's diagnosis **[medical record documentation required]**; **AND**
9. The requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below); **AND**
10. For requests for injection or infusion administration of the requested medication in an **inpatient or outpatient hospital setting,** Site of Care Criteria applies (outlined below)*

Duration of Approval: 365 days (1 year)

Continuation Criteria for Approval:

1. The patient was approved through Blue Cross NC initial criteria for approval; **OR**
2. The patient would have met initial criteria for approval at the time they started therapy; **AND**
3. The patient continues to have a PND score of IIIb or lower **[medical record documentation required]**; **OR**
4. The patient continues to have FAP stage 1 or 2 **[medical record documentation required]**; **AND**
5. The patient has demonstrated a positive clinical response (e.g., improved neurologic impairment, motor function, quality of life, and/or ambulation) while using the requested agent **[medical record documentation required]**; **AND**
6. The patient will NOT receive the requested agent in combination with any other TTR-directed therapy (e.g., acoramidis [Attruby], eplontersen [Wainua], inotersen [Tegsedi], tafamidis [Vyndamax], tafamidis meglumine [Vyndaqel], or vutrisiran [Amvuttra]) **[medical record documentation required]**; **AND**
7. The prescriber is a specialist in the area of the patient's diagnosis (e.g., geneticist, neurologist or specialist in the treatment of amyloidosis) or has consulted with a specialist in the area of the patient's diagnosis **[medical record documentation required]**; **AND**
8. The requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below); **AND**
9. For requests for injection or infusion administration of the requested medication in an **inpatient or outpatient hospital setting,** Site of Care Criteria applies (outlined below)*

Duration of Approval: 365 days (1 year)

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
patisiran (Onpattro®) intravenous (IV) infusion	Polyneuropathy of hATTR in patients ≥18 years old	Patients weighing <100 kg: 0.3 mg/kg IV every 3 weeks Patients weighing ≥100 kg: 30 mg IV every 3 weeks	J0222	5400

***Maximum units allowed for duration of approval**

***Site of Care Medical Necessity Criteria**

1. For requests for injection or infusion administration in an **inpatient setting**, the injection or infusion may be given if the above medical necessity criteria are met AND the inpatient admission is NOT for the sole purpose of administering the injection or infusion; **OR**
2. For requests for injection or infusion administration in an **outpatient hospital setting**, the injection or infusion may be given if the above medical necessity criteria are met AND ONE of the following must be met:
    a. History of mild adverse events that have not been successfully managed through mild pre-medication (e.g., diphenhydramine, acetaminophen, steroids, fluids, etc.); **OR**
    b. Inability to physically and cognitively adhere to the treatment schedule and regimen complexity; **OR**
    c. New to therapy, defined as initial injection or infusion OR less than 3 months since initial injection or infusion; **OR**
    d. Re-initiation of therapy, defined as ONE of the following:
        i. First injection or infusion after 6 months of no injections or infusions for drugs with an approved dosing interval less than 6 months duration; **OR**
        ii. First injection or infusion after at least a 1-month gap in therapy outside of the approved dosing interval for drugs requiring every 6 months dosing duration; **OR**
    e. Requirement of a change in the requested restricted product formulation; **AND**
3. If the Site of Care Medical Necessity Criteria in #1 or #2 above are not met, the injection or infusion will be administered in a **home-based infusion** or physician office setting with or without supervision by a certified healthcare professional.

References: all information referenced is from FDA package insert unless otherwise noted below.

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.

Policy Implementation/Update Information: Criteria and treatment protocols are reviewed annually by the Blue Cross NC P&T Committee, regardless of change. This policy is reviewed in Q4 annually.

October 2025: Criteria change: For hATTR-PN indication, added required trial and failure of eplontersen (Wainua) or diagnosis of hATTR with a mixed phenotype (exhibiting both polyneuropathy and cardiomyopathy). Adjusted list of TTR-directed therapies not to be used in combination and added geneticist to specialist list for clarity. Other minor adjustments made throughout policy for clarity with no change to policy intent. **Policy notification given 8/1/2025 for effective date 10/1/2025**.
Jannuary 2024: Criteria update: Updated requirement within initial and continuation sections that Onpattro will not be used in combination with newly approved Wainua (eplontersen).
October 2022: Criteria change: Added requirement within initial and continuation sections that Onpattro will not be used in combination with Amvuttra or Tegsedi. **Policy notification given 8/4/2022 for effective date 10/1/2022**.
October 2021: Criteria change: Added Site of Care medical necessity criteria. **Policy notification given 8/2/2021 for effective date 10/1/2021**.
June 2021: Criteria change: Added maximum units; medical policy formatting change. **Policy notification given 4/16/2021 for effective date 6/16/2021**.
*Further historical criteria changes and updates available upon request from Medical Policy and/or Corporate Pharmacy.