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

Restricted Product(s):

- vutrisiran (Amvuttra®) subcutaneous injection for administration by a healthcare professional

FDA Approved Use:

- For treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults
- For treatment of cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis in adults to reduce cardiovascular mortality, cardiovascular hospitalizations and urgent heart failure visits

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

iii. The patient has an FDA labeled contraindication to eplontersen (Wainua) **[medical record documentation required]**; **OR**
iv. The patient is diagnosed with hATTR with a mixed phenotype, exhibiting both polyneuropathy and cardiomyopathy **[medical record documentation required]**; **OR**

2. The patient has a diagnosis of **cardiomyopathy of wild-type or hereditary (variant) transthyretin-mediated amyloidosis (ATTR-CM)** as confirmed by testing (e.g., radionuclide bone scintigraphy with technetium-labeled bisphosphonates, monoclonal antibody studies, cardiac biopsy, genetic testing [*TTR* genotyping]) **[medical record documentation required]**; **AND**
    a. The patient is 18 years of age or older; **AND**
    b. The patient has clinical manifestations of cardiomyopathy (e.g., dyspnea, fatigue, orthostatic hypotension, syncope, peripheral edema) **[medical record documentation required]**; **AND**
    c. The patient has a history of heart failure (HF) with at least one prior hospitalization for HF or clinical evidence of HF (e.g., signs and symptoms of volume overload or elevated intracardiac pressures warranting diuretic treatment) **[medical record documentation required]**; **AND**
    d. The patient does NOT have NYHA Class IV HF, or NYHA Class III HF and considered high risk (e.g., an N-terminal prohormone of B-type natriuretic peptide (NT-proBNP) >3000 ng/L and estimated glomerular filtration rate (eGFR) <45 mL/min/1.73 m^2) **[medical record documentation required]**; **AND**
    e. ONE of the following:
        i. The patient has tried and had an inadequate response to at least ONE of the following agents: acoramidis (Attruby), tafamidis (Vyndamax), OR tafamidis meglumine (Vyndaqel) **[medical record documentation required]**; **OR**
        ii. The patient has an intolerance or hypersensitivity to ONE of the following agents: acoramidis (Attruby), tafamidis (Vyndamax), OR tafamidis meglumine (Vyndaqel) **[medical record documentation required]**; **OR**
        iii. The patient has an FDA labeled contraindication to ALL of the following agents: acoramidis (Attruby), tafamidis (Vyndamax), AND tafamidis meglumine (Vyndaqel) **[medical record documentation required]**; **OR**
        iv. The patient is diagnosed with hATTR with a mixed phenotype, exhibiting both polyneuropathy and cardiomyopathy **[medical record documentation required]**; **AND**

3. The patient has NOT had prior liver transplantation **[medical record documentation required]**; **AND**
4. The patient will NOT receive the requested agent in combination with any other TTR-directed therapy (e.g., acoramidis [Attruby], eplontersen [Wainua], inotersen [Tegsedi], patisiran [Onpattro], tafamidis [Vyndamax], or tafamidis meglumine [Vyndaqel]) **[medical record documentation required]**; **AND**

5. The prescriber is a specialist in the area of the patient's diagnosis (e.g., cardiologist, 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**
6. The requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below); **AND**
7. 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 has a diagnosis of **polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR-PN) [medical record documentation required]**; **AND**
    a. The patient continues to have a PND score of IIIb or lower **[medical record documentation required]**; **OR**
    b. The patient continues to have FAP stage 1 or 2 **[medical record documentation required]**; **AND**
    c. 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]**; **OR**
4. The patient has a diagnosis of **cardiomyopathy of wild-type or hereditary (variant) transthyretin-mediated amyloidosis (ATTR-CM) [medical record documentation required]**; **AND**
    a. The patient has demonstrated a positive clinical response (e.g., reduction in cardiovascular events [e.g., hospitalizations for cardiovascular causes or urgent visits for heart failure], improvement or stabilization in the 6-Minute Walk Test [6MWT], reduction in heart failure symptoms) while using the requested agent **[medical record documentation required]**; **AND**
5. The patient will NOT receive the requested agent in combination with any other TTR-directed therapy (e.g., acoramidis [Attruby], eplontersen [Wainua], inotersen [Tegsedi], patisiran [Onpattro], tafamidis [Vyndamax], or tafamidis meglumine [Vyndaqel]) **[medical record documentation required]**; **AND**
6. The prescriber is a specialist in the area of the patient's diagnosis (e.g., cardiologist, 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**
7. The requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below); **AND**
8. 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***
vutrisiran (Amvuttra®) subcutaneous (SC) injection	Polyneuropathy of hATTR in patients ≥18 years old Cardiomyopathy of ATTR in patients ≥18 years old	SC: 25 mg once every 3 months	J0225	100

***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, 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.
2. Ando Y, Coelho T, Berk JL, et al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. Orphanet J Rare Dis. 2013;8:31.
3. Fontana M, Berk JL, Gillmore JD, et al. HELIOS-B Trial Investigators. Vutrisiran in patients with transthyretin amyloidosis with cardiomyopathy. *N Engl J Med*. 2025 Jan 2;392(1):33-44.
4. Kittleson M, Ruberg F, Ambardekar A, et al. 2023 ACC Expert Consensus Decision Pathway on Comprehensive Multidisciplinary Care for the Patient With Cardiac Amyloidosis: A Report of the American College of Cardiology Solution Set Oversight Committee. *JACC.* 2023 Mar;81(11):1076-1126.

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 maximum units to more closely align with FDA label. **Policy notification given 8/1/2025 for effective date 10/1/2025**.
May 2025: Criteria change: Added newly approved indication for adults with cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis with corresponding criteria and required trial and failure of Attruby, Vyndamax, or Vyndaqel, or diagnosis of hATTR with a mixed phenotype (exhibiting both polyneuropathy and cardiomyopathy). Updated FDA label dosing table according to indication. Adjusted policy formatting and list of drugs not to be used in combination for clarity.
January 2024: Criteria update: Updated requirement within initial and continuation sections that Amvuttra will not be used in combination with newly approved Wainua (eplontersen) for clarity.
January 2023: Coding update: Added HCPCS code J0225 to dosing reference table effective 1/1/2023, deleted C9399, J3490, and J3590 termed 12/31/2022.
July 2022: Original medical policy criteria issued.