Neighborhood Health Plan OF RHODE ISLAND™
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Amvuttra (vutrisiran)
(Subcutaneous)

Effective Date: 01/01/2023
Review Date: 12/15/2022, 05/04/2023, 12/7/2023, 01/04/2024, 05/08/2024, 05/14/2025

Scope: Medicaid, Commercial, Medicare-Medicaid Plan (MMP)

I. Length of Authorization

Coverage will be provided for six months and may be renewed.

II. Dosing Limits

A. Max Units (per dose and over time) [HCPCS Unit]:

- 25 billable units (25 mg) every 3 months

III. Summary of Evidence

Amvuttra (vutrisiran) is a transthyretin-directed small interfering RNA (siRNA) indicated for the treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR-PN) in adults and cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) in adults. Amvuttra's approval is based on two phase 3 randomized, multi-center studies including 164 patients with hATTR-PN (HELIOS-A) and 654 patients with ATTR-CM (HELIOS-B). For hATTR-PN, Amvuttra demonstrated significant improvements in the modified Neuropathy Impairment Score +7 (mNIS+7), Norfolk Quality of Life-Diabetic Neuropathy (QoL-DN) total score, and 10-meter walk test at month 9 compared to placebo. For ATTR-CM, Amvuttra led to significant reduction in the risk of all-cause mortality and recurrent cardiovascular events (cardiovascular hospitalizations and urgent heart failure [UHF] visits) compared to placebo in the overall and monotherapy population of 28% and 33%, respectively during the double-blind treatment period of up to 36 months. The most common adverse effects of Amvuttra include pain in extremities, arthralgia, dyspnea, and decreases in vitamin A.

IV. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

MMP members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements

- Patient is at least 18 years of age; **AND**

Universal Criteria [1]

- Patient is receiving supplementation with vitamin A at the recommended daily allowance; **AND**
- Must not be used in combination with other transthyretin (TTR) reducing or stabilizing agents (e.g., eplontersen (Wainua), patisiran (Onpattro), acoramidis (Attruby), or tafamidis (Vyndaqel/Vyndamax)); **AND**
- Must be prescribed by or in consultation with a neurologist, cardiologist, or physician specializing in the treatment of amyloidosis related to hATTR or ATTR-CM; **AND**

Polyneuropathy due to Variant/Hereditary Transthyretin-Mediated (hATTR) Amyloidosis † Φ [1-7]

- Patient has a definitive diagnosis of hATTR amyloidosis as documented by amyloid deposition on tissue biopsy and identification of a pathogenic *TTR* variant using molecular genetic testing; **AND**
- Patient has polyneuropathy as demonstrated by at least TWO of the following criteria:
    - Subjective patient symptoms are suggestive of neuropathy
    - Abnormal nerve conduction studies are consistent with polyneuropathy
    - Abnormal neurological examination is suggestive of neuropathy; **AND**
- Patient's peripheral neuropathy is attributed to hATTR and other causes of neuropathy have been excluded; **AND**
- Baseline in strength/weakness has been documented using an objective clinical measuring tool (e.g., Medical Research Council (MRC) muscle strength, modified Neuropathy Impairment Scale+7 (mNIS+7) composite score, etc.); **AND**
- Coverage will not be provided in the following circumstances:
    - Prior or planned liver transplant
    - Severe renal impairment or end-stage renal disease
    - New York Heart Association (NYHA) heart failure classification >2
    - Other known causes of neuropathy (i.e. uncontrolled diabetes, sensorimotor or autonomic neuropathy not related to hATTR amyloidosis)
    - Primary or leptomeningeal amyloidosis

Cardiomyopathy of Wild Type or Variant/Hereditary Transthyretin-Mediated Amyloidosis (ATTR-CM) † Φ [1-8]

Authorization of 6 months may be granted for treatment of cardiomyopathy of wild type or variant/hereditary transthyretin-mediated amyloidosis (ATTR-CM) when all of the following criteria are met:

A. Documentation that the member exhibits clinical symptoms of cardiomyopathy and heart failure (e.g., dyspnea, fatigue, orthostatic hypotension, syncope, peripheral edema) classified as New York Heart Association (NYHA) class I, II, or III disease.
B. Documentation that cardiac involvement was confirmed by echocardiography or cardiac magnetic resonance imaging (e.g., end-diastolic interventricular septal wall thickness exceeding 12 mm).
C. The diagnosis is confirmed by one of the following:
    1. The member has documentation that meets both of the following:
        i. Presence of transthyretin amyloid deposits on analysis of biopsy from cardiac or noncardiac sites.
        ii. Presence of transthyretin precursor proteins was confirmed by immunohistochemical analysis, mass spectrometry, tissue staining, or polarized light microscopy.

2. The member has documentation that meets both of the following:
   i. Positive technetium-labeled bone scintigraphy tracing.
   ii. Systemic light chain amyloidosis is ruled out by a test showing absence of monoclonal proteins (serum kappa/lambda free light chain ratio, serum protein immunofixation, or urine protein immunofixation).

D. Documentation of genetic testing which confirms the presence of a mutation of the TTR gene for members with variant/hereditary ATTR (hATTR)
E. The member is not a liver transplant recipient.
F. For patients with ATTR-CM without evidence of polyneuropathy, the patient has had a trial and failure with a TTR stabilizer (e.g., acoramidis (Attruby) or tafamidis (Vyndaqel/Vyndamax) as evidenced by worsening of HF signs/symptoms, increase in NYHA class, CVH, decline in quality of life, etc.

† FDA Approved Indication(s); ‡ Compendium Recommended Indication(s) **Φ** Orphan Drug

V. Renewal Criteria [1-6]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria identified in section IV; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: ocular symptoms related to hypovitaminosis A, etc.; **AND**

Polyneuropathy due to Variant/Hereditary Transthyretin-Mediated (hATTR) Amyloidosis

- Disease response compared to pre-treatment baseline as evidenced by stabilization or improvement in one or more of the following:
  - Signs and symptoms of neuropathy (e.g., improved ambulation, improvement in neurologic symptom burden, improvement in activities of daily living)

Cardiomyopathy of Wild Type or Variant/Hereditary Transthyretin-Mediated Amyloidosis (ATTR-CM)

- Authorization of 6 months may be granted for the continued treatment of ATTR-CM when all of the following criteria are met:
  A. Documentation that the member must meet all initial authorization criteria.
  B. Documentation (e.g., medical records, chart notes) that the member must have demonstrated a beneficial response to treatment with acoramidis therapy [e.g., improvement in rate of disease progression as demonstrated by distance walked on the 6-minute walk test, the Kansas City Cardiomyopathy Questionnaire–Overall Summary (KCCQ-OS) score, cardiovascular-related hospitalizations, left ventricular stroke volume, N-terminal B-type natriuretic peptide (NT-proBNP) level].
  C. Documentation that the member has not progressed to NYHA class IV disease.

VI. Dosage/Administration [1]

Indication	Dose
hATTR polyneuropathy & ATTR cardiomyopathy	• The recommended dosage of Amvuttra is 25 mg administered by subcutaneous injection once every 3 months, administered by a healthcare professional.

VII. Billing Code/Availability Information

HCPCS Code:

- J0225 – Injection, vutrisiran, 1 mg; 1 billable unit = 1 mg

NDC:

- Amvuttra 25 mg/0.5 mL single-dose prefilled syringe: 71336-1003-xx

VIII. References

1. Amvuttra [package insert]. Cambridge, MA; Alnylam Pharmaceuticals, Inc., March 2025. Accessed April 2025.
2. 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. doi: 10.1056/NEJMoa1716153
3. 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
4. Ando Y, Coelho T, Berk JL, et al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. Orphanet J Rare Dis. 2013;8:31.
5. Sekijima Y. Hereditary Transthyretin Amyloidosis. 2001 Nov 5 [updated 2021 Jun 17]. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Mirzaa G, Amemiya A, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993–2021.
6. Luigetti M, Romano A, DiPaolantonio A, et al. Diagnosis and Treatment of Hereditary Transthyretin Amyloidosis (hATTR) Polyneuropathy: Current Perspectives on Improving Patient Care. Ther Clin Risk Manag. 2020; 16: 109–123.Published online 2020 Feb 21. doi: 10.2147/TCRM.S219979
7. Gonzalez-Duarte A, Adams D, Tournev I, et al. HELIOS-A: results from the phase 3 study of vutrisiran in patients with hereditary transthyretin-mediated amyloidosis with polyneuropathy. *J Am Coll Cardiol.* 2022 Mar, 79 (9_Supplement) 302. https://doi.org/10.1016/S0735-1097(22)01293-1
8. Fontana M, Berk JL, Gillmore JD, et al; HELIOS-B Trial Investigators and Collaborators. Vutrisiran in Patients with Transthyretin Amyloidosis with Cardiomyopathy. N Engl J Med. 2025 Jan 2;392(1):33-44. doi: 10.1056/NEJMoa2409134. Epub 2024 Aug 30. PMID: 39213194.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
E85.1	Neuropathic heredofamilial amyloidosis
E85.82	Wild-type transthyretin-related (ATTR) amyloidosis

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Articles (LCAs), and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCA/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Policy Rationale:

Amvuttra was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Amvuttra according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For INTEGRITY (Medicare-Medicaid Plan) members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.