Amvuttra (vutrisiran)
(Subcutaneous)

Document Number: SHP-0670

Last Review Date: 05/05/2025
Date of Origin: 07/05/2022
Dates Reviewed: 07/2022, 10/2023, 07/2024, 05/2025

I. Length of Authorization

Coverage will be provided for 12 months and may be renewed.

II. Dosing Limits

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

- 25 billable units (25 mg) every 3 months

III. Initial Approval Criteria [1]

Submission of supporting clinical documentation (including but not limited to medical records, chart notes, lab results, and confirmatory diagnostics) related to the medical necessity criteria is REQUIRED on all requests for authorizations. Records will be reviewed at the time of submission as part of the evaluation of this request. Please provide documentation related to diagnosis, step therapy, and clinical markers (i.e., genetic, and mutational testing) supporting initiation when applicable. Please provide documentation via direct upload through the PA web portal or by fax. Failure to submit the medical records may result in the denial of the request due to inability to establish medical necessity in accordance with policy guidelines.

Coverage is provided in the following conditions:

- 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., tafamidis, patisiran, acoramidis, etc.); **AND**

Polyneuropathy due to Hereditary Transthyretin-Mediated (hATTR) Amyloidosis † Φ [1,5-8]

- Patient has a definitive diagnosis of hATTR amyloidosis as documented by one of the following:
  - Amyloid deposition on tissue biopsy; **OR**
  - Identification of a pathogenic TTR variant using molecular genetic testing; **AND**
- Used for the treatment of polyneuropathy as demonstrated by at least TWO of the following criteria:

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- 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, etc.); **AND**
- Patient has not been the recipient of an orthotopic liver transplant (OLT)

Cardiomyopathy of Wild Type or Hereditary Transthyretin-Mediated Amyloidosis (ATTR-CM) † Φ [1,9]

- Patient has evidence of cardiac involvement by echocardiography with an end-diastolic interventricular septal wall thickness > 12 mm; **AND**
- Patient has a definitive diagnosis of Wild Type or Hereditary ATTR-CM as confirmed by laboratory testing (e.g., stannous pyrophosphate [PYP] scanning, monoclonal antibody studies, biopsy, scintigraphy, genetic testing [TTR genotyping]); **AND**
  - Patient has a medical history of heart failure which required at least 1 prior hospitalization; **OR**
  - Patient has clinical evidence of heart failure (with or without hospitalization) manifested by signs and symptoms of volume overload or elevated intracardiac pressure (e.g., elevated jugular venous pressure, shortness of breath or signs of pulmonary congestion on x-ray or auscultation, peripheral edema) which requires/required treatment with a diuretic; **AND**
- Patient has New York Heart Association (NYHA) Class I or II heart failure OR Class III heart failure that is not considered high risk (i.e., excludes patients with NYHA high risk Class III disease and Class IV disease); **AND**
- Patient has a baseline 6-minute walk-test (6MWT) distance of ≥150 meters

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

IV. Renewal Criteria [1]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: ocular symptoms related to vitamin A deficiency (e.g., night blindness), etc.; **AND**

Polyneuropathy due to Hereditary Transthyretin-Mediated (hATTR) Amyloidosis [1,5-8]

- 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

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- MRC muscle strength

Cardiomyopathy of Wild Type Transthyretin-Mediated Amyloidosis (ATTR-CM) [1,9]

- Disease response compared to pre-treatment baseline as evidenced by stabilization or improvement in one or more of the following:
  - Frequency of cardiovascular-related hospitalizations or urgent heart failure visits
  - Total distance walked during 6-minute walk test (6MWT)

V. 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. • ***Note:*** Amvuttra should be administered by a healthcare professional.

VI. 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

VII. 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, Nakamura K. Hereditary Transthyretin Amyloidosis. In: Adam MP, Feldman J, Mirzaa G, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993–2024. Initial Posting: November 5, 2001; Last Update: May 30, 2024. Accessed June 11, 2024. https://www.ncbi.nlm.nih.gov/books/NBK1194/.
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

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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. Adams D, Tournev IL, Taylor MS, et al; HELIOS-A Collaborators. Efficacy and safety of vutrisiran for patients with hereditary transthyretin-mediated amyloidosis with polyneuropathy: a randomized clinical trial. Amyloid. 2023 Mar;30(1):1-9. doi: 10.1080/13506129.2022.2091985. Epub 2022 Jul 23. PMID: 35875890.
9. 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)

The preceding information is intended for non-Medicare coverage determinations. 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 Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied 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

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Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
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

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