Amvuttra (vutrisiran)
(Subcutaneous)

Document Number: EOCCO-0670

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I. Length of Authorization

Initial coverage will be provided for 6 months and may be renewed annually thereafter.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Amvuttra 25 mg/0.5 mL single-dose prefilled syringe: 1 syringe every 3 months

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

- 25 billable units (25 mg) every 3 months

III. Initial Approval Criteria [1]

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., inotersen, tafamidis, patisiran, etc.); **AND**

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

- Patient has a definitive diagnosis of hATTR amyloidosis as documented in a proband with suggestive findings (including imaging or histopathology findings of amyloidosis) and a heterozygous pathogenic (or likely pathogenic) variant in *TTR* identified by molecular genetic testing; **AND**
- Used for the treatment of 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, etc.); **AND**
- Patient has not been the recipient of an orthotopic liver transplant (OLT)

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

IV. Renewal Criteria [1,5-8]

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**
- 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
  - MRC muscle strength

V. Dosage/Administration [1]

Indication	Dose
hATTR polyneuropathy	• 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., February 2023. Accessed May 2024.

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
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.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
E85.1	Neuropathic heredofamilial 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
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