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

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. 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. Summary of Evidence

Amvuttra (vutrisiran) is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR-PN) in adults. The drug is a small interfering RNA (siRNA) injection and the third FDA-approved therapy for hATTR-PN. Amvuttra was approved based on positive results from the phase 3 HELIOS-A clinical trial, in which Amvuttra treatment resulted in statistically significant improvements on multiple polyneuropathy scales compared with placebo at nine months. Amvuttra's dosing interval and route of administration, as well as side effect profile, is advantageous in comparison to the other agents approved for the same indication.

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 agents (e.g., Onpattro (patisiran), Amvuttra (vutrisiran), Vyndaqel/Vyndamax (tafamadis), etc.); **AND**

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

- Must be prescribed by or in consultation with a neurologist, or physician specializing in the treatment of amyloidosis related to hATTR/FAP; AND
- Patient has a definitive diagnosis of hATTR amyloidosis/FAP 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/FAP 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 hATTR (hATTR-CM)

† 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 III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: ocular symptoms related to hypovitaminosis A, 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 (e.g., improved ambulation, improvement in neurologic symptom burden, improvement in activities of daily living)

VI. Documented improvement of clinical response compared to baseline (e.g., MRC muscle strength, modified Neuropathy Impairment Scale+7 (mNIS+7) composite score, Norfolk Quality of Life-Diabetic Neuropathy (QoL-DN) total score, etc.) Dosage/Administration [1]

Indication	Dose
hATTR polyneuropathy	• 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., January 2023. Accessed April 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. 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

Appendix 1 – Covered Diagnosis Codes

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