Medical Policy:

Amvuttra™ (vutrisiran) subcutaneous solution

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.359	August 25, 2025	August 11, 2022

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The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as "EmblemHealth"), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

Definitions

Amvuttra™ is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults. Vutrisiran is a double-stranded small interfering ribonucleic acid (siRNA)-N-acetylgalactosamine (GalNAc) conjugate that causes degradation of mutant and wild-type transthyretin (TTR) messenger RNA (mRNA) through RNA interference, which results in a reduction of serum TTR protein and TTR protein deposits in tissues.

Length of Authorization

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

Dosing Limits [Medical Benefit]

Quantity Limits: Four injections per year (25 billable units (25 mg) every 3 months)

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

- 25 billable units (25 mg) every 3 months

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Guideline

I. INITIAL APPROVAL CRITERIA

1. **Polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR).** Approve if patient meets all of the following:
   A. Patient is 18 years and older; **AND**
   B. Patient is receiving supplementation with vitamin A at the recommended daily allowance**; AND**
   C. 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**
   D. Used for the treatment of polyneuropathy as demonstrated by at least **TWO** of the following criteria:
      i. Subjective patient symptoms are suggestive of neuropathy
      ii. Abnormal nerve conduction studies are consistent with polyneuropathy
      iii. Abnormal neurological examination is suggestive of neuropathy; **AND**
   E. Patient's peripheral neuropathy is attributed to hATTR and other causes of neuropathy have been excluded; **AND**
   F. Baseline in strength/weakness has been documented using an objective clinical measuring tool *Examples include: Medical Research Council (MRC), muscle strength, etc.*
   G. Patient does not have a history of orthotopic liver transplantation (OLT)

Cardiomyopathy of Wild Type or Hereditary Transthyretin-Mediated Amyloidosis (ATTR-CM) † Φ

A. Patient has evidence of cardiac involvement by echocardiography with an end-diastolic interventricular septal wall thickness > 12 mm; **AND**
B. 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**
   i. Patient has a medical history of heart failure which required at least 1 prior hospitalization; **OR**
   ii. 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**
C. 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**
D. Patient has a baseline 6-minute walk-test (6MWT) distance of ≥150 meters

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

II. RENEWAL CRITERIA

A. The initial criteria must continue to be met; **AND**
B. Absence of unacceptable toxicity from the drug; **AND**

Polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR)

A. Disease response compared to pre-treatment baseline as evidenced by stabilization or improvement in one or more of the following:
   i. Signs and symptoms of neuropathy
   ii. MRC muscle strength

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Cardiomyopathy of Wild Type Transthyretin-Mediated Amyloidosis (ATTR-CM)

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

Limitations/Exclusions

1. Concomitant Use With Onpattro (patisiran intravenous infusion), Tegsedi (inotersen subcutaneous injection), Wainua (eplontersen subcutaneous injection), or a Tafamidis Product.
   Note: Examples of tafamidis products are Vyndaqel and Vyndamax.

Applicable Procedure Codes

Code	Description
J0225	Injection, vutrisiran 1mg

Applicable NDCs

Code	Description
71336-1003-01	Amvuttra 25mg/0.5mL subcutaneous solution

ICD-10 Diagnoses

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

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	8/25/2025	Update: Length of Authorization: removed 12 months and updated to: “6 months and may be renewed annually thereafter.” Added the following to dosing limits: “Max Units (per dose and over time) [HCPCS Unit]: 25 billable units (25 mg) every 3 months “ Initial Criteria: Polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR) Updated liver transplantation to: orthotopic liver transplantation (OLT) Removed: The medication is prescribed by, or in consultation with, a neurologist, geneticist, or a physician who specializes in the treatment of amyloidosis.” Added: “Cardiomyopathy of Wild Type or Hereditary Transthyretin-Mediated Amyloidosis (ATTR-CM) † Φ and all criteria. Renewal Criteria: Polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR) Removed the following to reword: “Documentation of clinical response to therapy, such as an improvement, stabilization, or slowing of progression of hATTR-PN manifestations “ reworded to: “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”

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		Added: “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) “ Added E85.82
EmblemHealth & ConnectiCare	2/18/2025	Annual Review: Added (25 billable units (25 mg) every 3 months to dosing limits. Criteria guidelines: Removed: Patient has a transthyretin mutation as confirmed by genetic testing; AND Patient has symptomatic polyneuropathy; AND *Note: Examples of symptomatic polyneuropathy include reduced motor strength/coordination, and impaired sensation (e.g., pain, temperature, vibration, touch). Examples of assessments for symptomatic disease include history and clinical exam, electromyography, or nerve conduction velocity testing.*Added in Patient is receiving supplementation with vitamin A at the recommended daily allowance; AND 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 *Examples include Medical Research Council (MRC), muscle strength, etc.* Added into renewal criteria: Absence of unacceptable toxicity from the drug
EmblemHealth & ConnectiCare	4/22/2024	Annual Review: Added Limitations/Exclusions
EmblemHealth & ConnectiCare	8/4/2023	Annual Review: Removed Codes: J3490 and C9399. Added code J0225
EmblemHealth & ConnectiCare	8/11/2022	New Policy

References

1. Product Information: AMVUTTRA™ subcutaneous injection, vutrisiran subcutaneous injection. Alnylam Pharmaceuticals Inc (per FDA), Cambridge, MA, 2022

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