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Section:	Prescription Drugs	**Effective Date:**	April 1, 2026
Subsection:	Neuromuscular Drugs	**Original Policy Date:**	July 8, 2022
Subject:	Amvuttra	**Page:**	1 of 7

Last Review Date: March 6, 2026

Amvuttra

Description

Amvuttra (vutrisiran)

Background

Amvuttra (vutrisiran) is a double-stranded siRNA-GaINAc conjugate that causes degradation of mutant and wild-type TTR mRNA through RNA interference, which results in a reduction of serum TTR protein and TTR protein deposits in tissues (1).

Regulatory Status

FDA-approved indication: Amvuttra is a transthyretin-directed small interfering RNA indicated for the treatment of: (1)

- the polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis in adults.
- the cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis in adults to reduce cardiovascular mortality, cardiovascular hospitalizations, and urgent heart failure visits.

Amvuttra is for subcutaneous use only and should be administered by a healthcare professional (1).

Amvuttra treatment leads to a decrease in serum vitamin A levels. Supplementation at the recommended daily allowance of vitamin A is advised for patients taking Amvuttra. Higher doses than recommended daily allowance of vitamin A should not be given to try to achieve normal serum vitamin A levels during treatment with Amvuttra, as serum vitamin A levels do not

reflect the total vitamin A in the body. Patients should be referred to an ophthalmologist if they develop ocular symptoms suggestive of vitamin A deficiency (e.g., night blindness) (1).

The safety and effectiveness of Amvuttra in pediatric patients have not been established (1).

Related policies
Onpattro, Tegsedi, Vyndaqel/Vyndamax, Wainua

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Amvuttra may be considered **medically necessary** if the conditions indicated below are met.

Amvuttra may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age and older

Diagnosis

Patient must have the following:

Polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis

AND ALL of the following:

1. Diagnosis of hATTR confirmed by a genetic test **OR** a tissue biopsy showing amyloid deposition
2. Patient must have **ONE** of the following baseline scores:
    a. Polyneuropathy disability (PND) score ≤ IIIb (see Appendix 1)
    b. FAP Stage 1 or 2 (see Appendix 2)
3. Will be administered by a healthcare professional
4. Prescriber agrees to supplement the patient with the recommended daily allowance of Vitamin A if indicated
5. Patient has **NONE** of the following:
    a. New York Heart Association (NYHA) class III or IV heart failure
    b. Sensorimotor or autonomic neuropathy not related to hATTR amyloidosis (monoclonal gammopathy, autoimmune disease, etc.)

c. Prior liver transplantation

6. Prescribed by or in consultation with a neurologist, or a specialist in the treatment of the patient's diagnosis
7. **NO** dual therapy with another Prior Authorization (PA) medication for polyneuropathy caused by hATTR amyloidosis (see Appendix 3)

Age 18 years of age or older

Diagnosis

Patient must have the following:

Cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM)

AND ALL of the following:

1. Diagnosis has been confirmed by a genetic test **OR** tissue biopsy showing amyloid deposition
2. Clinical signs and symptoms of cardiac involvement by **ALL** of the following:
    a. End-diastolic interventricular septal wall thickness > 12 mm by echocardiography
    b. History of heart failure with at least one hospitalization for heart failure **OR** clinical evidence of heart failure with signs and symptoms of volume overload or elevated intracardiac pressures requiring treatment with a diuretic for improvement
    c. Baseline NT-proBNP ≥ 600 pg/mL
3. **NO** NYHA class IV heart failure
4. **NO** light chain amyloidosis

Prior – Approval *Renewal* Requirements

Age 18 years of age and older

Diagnosis

Patient must have the following:

Polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis

AND ALL of the following:

1. Patient condition has improved or stabilized
2. Will be administered by a healthcare professional
3. Prescriber agrees to supplement the patient with the recommended daily allowance of Vitamin A if indicated
4. **NO** dual therapy with another Prior Authorization (PA) medication for polyneuropathy caused by hATTR amyloidosis (see Appendix 3)

Age 18 years of age or older

Diagnosis

Patient must have the following:

Cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM)

AND the following:

1. Patient's condition has improved or stabilized [e.g., reduced number of hospitalizations, improved 6-minute walk test (6-MWT), or improved Kansas City Cardiomyopathy Questionnaire Overall Summary Score (KCCQ-OS)]

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity 1 pre-filled syringe per 90 days

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary
Amvuttra (vutrisiran) is a transthyretin-directed small interfering RNA. Amvuttra is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis and cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis. It is recommended that patients treated with Amvuttra be supplemented with the recommended daily allowance of vitamin A. The safety and effectiveness of Amvuttra in pediatric patients have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Amvuttra while maintaining optimal therapeutic outcomes.

References

1. Amvuttra [package insert]. Cambridge, MA: Alnylam Pharmaceuticals, Inc.; March 2025.
2. Fontana M, Berk JL, Gillmore JD, et al. Vutirsiran in patients with transthyretin amyloidosis with cardiomyopathy. N. Engl. J Med. 2025; 392:33-44. DOI: 10.1056/NEJMoa2409134

Policy History

Date	Action
July 2022	Addition to PA
August 2022	Revised criteria to align with BCBS association criteria: Addition of Appendix 1, 2 and 3; to align with BCBS association criteria: added requirement of 1. Diagnosis of hATTR confirmed by a genetic test OR documentation of tissue biopsy showing amyloid deposition; 3. Patient must have ONE of the following baseline scores:a. Polyneuropathy disability (PND) score ≤ IIIb (see appendix 1) b. FAP Stage 1 or 2 (see appendix 2);4.Patient has NONE of the following: a.New York Heart Association (NYHA) class III or IV heart failure b. Sensorimotor or autonomic neuropathy not related to hATTR amyloidosis (monoclonal gammopathy, autoimmune disease, etc.)c. Prior liver transplantation; 8. Prescribed by or in consultation with a neurologist, or a specialist in the treatment of the patient's diagnosis; revised continuation requirement to include improvement or stabilization in patient condition
September 2022	Annual review
March 2023	Annual review
December 2023	Annual review and reference update

March 2024	Annual review
June 2024	Annual review
December 2024	Annual review
March 2025	Annual review
April 2025	Per PI update, added indication of cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis
September 2025	Annual review
March 2026	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 6, 2026 and is effective on April 1, 2026.

Appendix 1 - Polyneuropathy Disability (PND) Severity Scoring System

Polyneuropathy Disability (PND) Score	
Stage 0	No impairment
Stage I	Sensory disturbances but preserved walking capability
Stage II	Impaired walking capability but ability to walk without a stick or crutches
Stage IIIA	Walking only with the help of one stick or crutches
Stage IIIB	Walking only with the help of two sticks or crutches
Stage IV	Confined to a wheelchair or bedridden

Appendix 2 - FAP Stage Severity Scoring System

FAP Stage	
Stage 0	No symptoms
Stage I	Unimpaired ambulation; mostly mild sensory, motor, and autonomic neuropathy in the lower limbs
Stage II	Assistance with ambulation required; mostly moderate impairment progression to the lower limbs, upper limbs, and trunk
Stage III	Wheelchair bound or bedridden; severe sensory, motor, and autonomic involvement of all limbs

Appendix 3 - List of PA Medications for Polyneuropathy caused by hATTR Amyloidosis

Generic Name	Brand Name
eplontersen	Wainua
inotersen	Tegsedi
patisiran	Onpattro
vutrisiran	Amvuttra