# Amvuttra (vutrisiran)
## PAM – 067

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| **Iowa Medicaid Program** | Prior Authorization | **Effective Date** | 01/01/2023 |
| **Revision Number** | 3 | **Last Reviewed** | 04/17/2026 |
| **Reviewed By** | Medicaid Medical Director | **Next Review** | 01/15/2027 |
| **Approved By** | Medicaid Clinical Advisory Committee | **Approved Date** | 01/19/2024 |

## Overview

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|---|---|
| Medication: [1] | Vutrisiran |
| Brand Name: | Amvuttra® |
| Pharmacologic Category: | Transthyretin-directed small interfering RNA |
| FDA-Approved Indication(s): | 1. Treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR-PN) in adults<br>2. Treatment of the cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) in adults to reduce cardiovascular mortality, cardiovascular hospitalizations, and urgent heart failure visits.<br>▶ **NEW** indication: FDA-approved 3/20/2025 |
| How Supplied: | Single-dose prefilled syringe, 25 mg/0.5 mL |
| Dosage and Administration: | • 25 mg via subcutaneous injection once every 3 months<br>• Should only be administered by a healthcare professional |
| Benefit Category: | Medical |

## Descriptive Narrative

Hereditary transthyretin-mediated amyloidosis (hATTR amyloidosis) is an autosomal dominant disorder (>120 TTR gene mutations known) that is characterized by the slowly progressive buildup of amyloid protein in the peripheral and central nervous systems, heart, kidneys, eyes, bone, and gastrointestinal tract. Transthyretin (TTR) is a tetrameric protein primarily produced in hepatocytes. The disease is caused by genetic mutations in the TTR gene that lead the tetrameric TTR protein to break into monomeric units that misfold and aggregate as amyloid fibril deposits.

There are three general forms of the disease, although patients can have overlapping symptoms from all three forms. The neuropathic form (hereditary TTR amyloidosis polyneuropathy [hATTR-PN], also known as transthyretin familial amyloid polyneuropathy [TTRFAP]), is defined by the presence of sensorimotor peripheral neuropathy (with symptoms of numbness, pain, and weakness), focal nerve lesions (e.g., carpal tunnel syndrome), autonomic dysfunction (e.g.,

orthostatic hypotension, gastrointestinal dysfunction), vitreous opacity of the eye, and glaucoma. The leptomeningeal form is defined by the presence of stroke, intracranial hemorrhage, hydrocephalus, ataxia, spastic paralysis, seizures, dementia, psychosis, and vision impairment. The cardiac form is defined by the presence of arrhythmia, cardiomegaly, heart failure, and death.

In hATTR amyloidosis, misfolding of the TTR protein leads to its aggregation and the formation of amyloid fibrils, which interfere with the normal function of affected organ systems, including the peripheral nervous system (hereditary TTR amyloidosis polyneuropathy [hATTR-PN]. [2] Approximately 100 to 2500 individuals are estimated to have hATTR-PN in the United States.[3]

Cardiac amyloidosis is a rare form of cardiomyopathy caused by amyloid fibril deposition in the extracellular space of the heart. It can present with cardiac signs or symptoms or may be diagnosed as the result of screening in patients who manifest extracardiac signs of amyloidosis. Approximately 95 percent of cases of cardiac amyloidosis are caused by the deposition of transthyretin (TTR) or immunoglobulin light chains.

1. **Transthyretin amyloidosis (ATTR amyloidosis)** – Transthyretin amyloidosis results from the misfolding and deposition of transthyretin (TTR, formerly known as prealbumin), a tetrameric protein synthesized by the liver that normally functions to transport thyroid hormone and retinol (vitamin A). ATTR amyloidosis can be further divided into two subtypes:
   - **Wild-type amyloidosis (wtATTR amyloidosis)** – Wild-type transthyretin amyloidosis (previously known as senile systemic amyloidosis) is caused by the deposition of misfolded wild-type (normal) transthyretin. The mechanism by which normal transthyretin causes pathogenic deposits is unclear.
   - **Hereditary amyloidosis (hATTR amyloidosis)** – Hereditary transthyretin amyloidosis is caused by gene mutations in the transthyretin gene (*TTR*) that predispose the tetrameric structure of transthyretin to instability, misfolding, and deposition. The typical transmission of hATTR is autosomal dominant inheritance with variable penetrance, and there are more than 120 known mutations of *TTR* associated with hATTR amyloidosis.
2. **Light chain amyloidosis (AL amyloidosis)** – Light chain amyloidosis (AL amyloidosis; also known as primary systemic amyloidosis) results from deposition of misfolded immunoglobulin light chains from a plasma cell dyscrasia.

**Other types of amyloid** – Rare causes of cardiac amyloidosis include serum amyloid A amyloidosis (AA), hereditary apolipoprotein A-1 (AApoA-1), and apolipoprotein A-4 (AApoA-4) amyloidosis.

The usual age of onset of symptoms and disease distribution varies among the various types of amyloidosis. Patients with transthyretin cardiac amyloidosis (ATTR amyloidosis) typically present at age 60 years or older, and most commonly at older than 70 years of age. Various transthyretin mutations are associated with differing ages of onset (ranging from 30 to 70 years) and differing risks of cardiomyopathy.[4]

## Guidelines

*Guideline of transthyretin-related hereditary amyloidosis for clinicians*, published in 2013, was written to help physicians better understand transthyretin amyloidosis. It includes guidance on making a definitive diagnosis, explains methods for disease staging and evaluation of disease progression, and discusses symptom mitigation and treatment strategies, including liver transplant and several pharmacotherapies that have shown promise in clinical trials. Some of the pharmacotherapies in clinical trials (such as Amvuttra®) have been approved by the FDA since the 2013 publication of these guidelines.[5]

In 2023, the American College of Cardiology (ACC) published an Expert Consensus Decision Pathway on Comprehensive Multidisciplinary Care for the Patient with Cardiac Amyloidosis. This pathway was endorsed by the American Association of Neuromuscular & Electrodiagnostic Medicine, Heart Failure Society of America, and International Society of Amyloidosis. The American Academy of Neurology affirmed the value of this statement. At the time of publication, tafamidis (oral therapy, available as Vyndaqel® or Vyndamax®) was the only medication approved by the FDA for treatment of ATTR cardiac amyloidosis (Amvuttra® had not yet been FDA-approved for this indication).[6]

## Criteria

Prior authorization is required.

### 1. Polyneuropathy of Hereditary Transthyretin-Mediated Amyloidosis

Amvuttra® is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of hereditary transthyretin-mediated amyloidosis with polyneuropathy (hATTR-PN), as confirmed by:
    a. Presence of a transthyretin (TTR) gene mutation; **AND**
    b. Nerve biopsy which is positive for amyloid deposits (or medical justification is provided as to why treatment should be initiated despite a negative biopsy or no biopsy); **AND**
2. Member has clinical signs and symptoms of polyneuropathy (i.e., weakness, sensory loss, decreased motor strength, decreased gait speed); **AND**
3. Member is 18 years of age or older; **AND**
4. Member has not had a prior liver transplant; **AND**
5. Amvuttra® is not prescribed concurrently with Onpattro® or Tegsedi™; **AND**
6. Prescribed by, or in consultation with, a neurologist; **AND**
7. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 25 mg once every 3 months; or
    b. Regimen is supported by clinical practice guidelines. Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

## 2. Cardiomyopathy of Wild-Type or Hereditary Transthyretin-Mediated Amyloidosis (ATTR-CM)

Amvuttra® is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of transthyretin (ATTR) amyloidosis (classified as either hereditary or wild-type ATTR) with cardiomyopathy, as confirmed by:
   a. Presence of a transthyretin (TTR) gene mutation; **AND**
   b. Nerve biopsy which is positive for amyloid deposits (or medical justification is provided as to why treatment should be initiated despite a negative biopsy or no biopsy); **AND**
2. Member has a history of heart failure, with at least one prior hospitalization for heart failure OR clinical evidence of heart failure; **AND**
3. Member is 18 years of age or older; **AND**
4. Member does **NOT** have New York Heart Association class IV disease; **AND**
5. Prescribed by, or in consultation with, a cardiologist; **AND**
6. Request meets one of the following (a or b):
   a. Regimen prescribed does not exceed 25 mg once every 3 months; or
   b. Regimen is supported by clinical practice guidelines. Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

## Continuation Criteria – all above indications

Amvuttra® is considered medically necessary for continuation of therapy when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Diagnosis of either (a or b):
   a. hereditary transthyretin-mediated amyloidosis with polyneuropathy (hATTR-PN); or,
   b. cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM); **AND**
3. Documentation of positive clinical response to therapy, as demonstrated by clinically significant improvement or stabilization in clinical signs and symptoms of the disease (e.g., motor strength, ambulation, neurological symptom burden, quality of life, activities of daily living); **AND**
4. Amvuttra® is not prescribed concurrently with Onpattro® or Tegsedi™; **AND**
5. Prescribed by, or in consultation with, a neurologist (for hATTR-PN) or a cardiologist (for ATTR-CM); **AND**
6. Request meets one of the following (a or b):
   a. Regimen prescribed does not exceed 25 mg once every 3 months; or
   b. Regimen is supported by clinical practice guidelines. Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

## Approval Duration and Quantity Limits

| | Initial Authorization | Subsequent Authorization(s) |
|---|---|---|
| Approval Duration | 6 months | 12 months |
| Quantity Limits | 25 mg every 3 months | 25 mg every 3 months |

## Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

| HCPCS | Description |
|---|---|
| J0225 | Injection, vutrisiran, 1 mg |

| ICD-10 | Description |
|---|---|
| E85.1 | Neuropathic heredofamilial amyloidosis |
| E85.82 | Wild-type transthyretin-related (ATTR) amyloidosis |
| E85.4 | Organ-limited amyloidosis |

| NDC (Strength) | Labeler | Dosage | Pkg Size | Pkg Qty | Units/ Pkg |
|---|---|---|---|---|---|
| 71336-1003-01 (single-dose syringe, 25 mg/0.5 mL) | Alnylam Pharmaceuticals, Inc. (71336) | 1 mg | 1 | EA | 25 |

## Compliance

1. Should conflict exist between the policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations.

Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

## References


[1] Amvuttra® prescribing information (03/2025). Alnylam Pharmaceuticals, Inc.: Cambridge, MA. Available online: www.amvuttrahcp.com. Accessed January 22, 2026.

[2] Vutrisiran Clinical Review (NDA 215515). U.S. Food and Drug Administration: Center for Drug Evaluation and Research (CDER). Application Number 215515Orig1s000. Review completed June 13, 2022. Available online at www.accessdata.fda.gov/drugsatfda_docs/nda/2022/215515 Orig1s000 MedR.pdf. Accessed December 18, 2023.

[3] Schmidt HH, et al. Estimating the global prevalence of transthyretin familial amyloid polyneuropathy. Muscle Nerve. 2018 May;57(5):829-837. Epub 2018 Feb 1. PMID: 29211930; PMCID: PMC5947118.

[4] Fontana M. Cardiac amyloidosis: Epidemiology, clinical manifestations, and diagnosis. Yeon SB, ed. UpToDate. Waltham, MA: UpToDate, Inc. www.uptodate.com. Accessed February 18, 2026.

[5] Ando Y, Coelho T, et al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. Orphanet J Rare Dis. 2013 Feb 20;8:31. PMID: 23425518; PMCID: PMC3584981.

[6] Writing Committee; Kittleson MM, Ruberg FL, et al. 2023 ACC Expert Consensus Decision Pathway on Comprehensive Multidisciplinary Care for the Patient With Cardiac Amyloidosis: A Report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol. 2023 Mar 21;81(11):1076-1126. Epub 2023 Jan 23. Erratum in: J Am Coll Cardiol. 2023 Mar 21;81(11):1135. PMID: 36697326.


Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

## Criteria Change History

| Change Date | Changed By | Description of Change | Version |
|---|---|---|---|
| [mm/dd/yyyy] | CAC | | |
| **Signature** | | | |

| Change Date | Changed By | Description of Change | Version |
|---|---|---|---|
| [mm/dd/yyyy] | CAC | | |
| **Signature** | | | |

| Change Date | Changed By | Description of Change | Version |
|---|---|---|---|
| 04/17/2026 | CAC | Annual review. New indication for treatment of the cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis in adults (ATTR-CM) (FDA-approved 3/20/2025). Added to Overview table, Descriptive Narrative, Guidelines, and Coverage Criteria. Updated references. | 3 |
| **Signature** William (Bill) Jagiello, DO | |  | |

| Change Date | Changed By | Description of Change | Version |
|---|---|---|---|
| 01/17/2025 | CAC | Annual review. No changes. | 2 |
| **Signature** William (Bill) Jagiello, DO | |  | |

| Change Date | Changed By | Description of Change | Version |
|---|---|---|---|
| 01/19/2024 | CAC | Criteria implementation. | 1 |
| **Signature** William (Bill) Jagiello, DO | |  | |

CAC = Medicaid Clinical Advisory Committee