Medical Drug Clinical Criteria

Subject:	Amvuttra (vutrisiran)		
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Table of Contents

Overview

This document addresses the use of Amvuttra (vutrisiran), a small interfering RNA approved by the Food and Drug Administration (FDA) for the treatment of polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis in adults. hATTR amyloidosis was formerly known as familial amyloid polyneuropathy (FAP). Amvuttra is also FDA approved for the treatment of cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) in adults to reduce cardiovascular mortality, cardiovascular hospitalizations and urgent heart failure visits.

Transthyretin-mediated amyloidosis is a multisystemic, progressive disease characterized by extracellular deposition of amyloid fibrils composed of misfolded transthyretin (TTR), a plasma transport protein produced predominantly by the liver. Amyloid fibrils accumulate in various organs and tissues including the heart, kidney, gastrointestinal tract, and peripheral nerves, resulting in clinical manifestations such as polyneuropathy and cardiomyopathy. Potential symptoms associated with transthyretin-mediated amyloidosis include but are not limited to muscle weakness, difficulty ambulating, impaired balance, orthostatic hypotension, disturbances in GI mobility, heart failure, arrhythmias, and sudden death due to severe conduction disorders.

To effectively quantify the overall disease burden in individuals with transthyretin-mediated amyloidosis, it is essential to consider the constellation of symptoms and the multisystemic nature of the disease. This requires using a variety of assessments. For evaluating neuropathy, clinical tests such as the Neuropathy Impairment Score (NIS) and the Polyneuropathy Disability (PND) Score are commonly used. Amvuttra has been studied in individuals with hereditary transthyretin-mediated amyloidosis who have mild to moderate polyneuropathy, which can be characterized by the ability to ambulate with or without assistance. Additionally, consensus guidelines offer direction for evaluating and diagnosing cardiomyopathy. Experts recommend using non-invasive radionuclide scintigraphy or performing endomyocardial or extracardiac biopsy to confirm a diagnosis of transthyretin-mediated amyloid cardiomyopathy.

The efficacy of Amvuttra was assessed in a randomized, open-label trial in adults with hereditary transthyretin amyloidosis with polyneuropathy. Study participants had a Neuropathy Impairment Score (NIS) of 5-130 (NIS scale ranges from 0-244), a polyneuropathy disability score of IIIb or lower and a TTR mutation confirmed by genotyping. Key exclusion criteria were previous liver transplant, New York Heart Association (NYHA) class III or IV heart failure, severe renal impairment or end-stage renal disease, moderate or severe hepatic impairment and other causes of polyneuropathy unrelated to hATTR amyloidosis. The primary efficacy assessment was reported to favor Amvuttra over placebo, but the clinical trial results are unpublished.

The efficacy of Amvuttra for cardiomyopathy was assessed in a randomized, double-blind, placebo-controlled trial in 654 individuals with wild-type or hereditary transthyretin-mediated amyloid cardiomyopathy. The trial included individuals with New York Heart Association (NYHA) class I, II or III heart failure symptoms and allowed for use in combination with tafamidis. Amvuttra demonstrated a significant reduction in the risk of all-cause mortality and recurrent cardiovascular hospitalizations and urgent heart failure visits compared to placebo in the overall and monotherapy population of 28% and 33%, respectively.

Amvuttra is administered as a subcutaneous injection by a healthcare provider every three months. Treatment with Amvuttra leads to a decrease in serum vitamin A levels. Individuals should be advised to take vitamin A supplementation at the recommended daily allowance while receiving Amvuttra therapy.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Amvuttra (vutrisiran)

Initial requests for Amvuttra (vutrisiran) for polyneuropathy of transthyretin-mediated amyloidosis may be approved if the following criteria are met:

I. Individual has a diagnosis of hereditary transthyretin (hATTR) amyloidosis or familial amyloid polyneuropathy (FAP); **AND**
II. Documentation is provided that individual has a TTR mutation verified by genotyping (NCT 03759379); **AND**
III. Documentation is provided that individual has associated mild to moderate polyneuropathy (NCT 03759379).

Continuation requests for Amvuttra (vutrisiran) for polyneuropathy of transthyretin-mediated amyloidosis may be approved if the following criterion is met:

I. Documentation is provided that there is clinically significant improvement or stabilization in clinical signs and symptoms of disease (including but not limited to improved ambulation, improvement in neurologic symptom burden, improvement in activities of daily living).

Initial requests for Amvuttra (vutrisiran) for cardiomyopathy of transthyretin-mediated amyloidosis may be approved if the following criteria are met:

I. Individual has a diagnosis of wild-type or hereditary transthyretin amyloid cardiomyopathy; **AND**
II. Documentation is provided that diagnosis has been demonstrated by (Dorbala 2021, Kittleson 2023):
    A. Endomyocardial or extracardiac biopsy; **OR**
    B. Both of the following:
        1. Radionuclide scintigraphy (99mTc-PYP/DPD/HMDP) with grade 2 or 3 uptake; **AND**
        2. Absence of monoclonal protein on serum free light chain assay and serum and urine immunofixation; **AND**
III. Individual is using for the treatment of New York Heart Association class I, II or III heart failure symptoms.

Continuation requests for Amvuttra (vutrisiran) for cardiomyopathy of transthyretin-mediated amyloidosis may be approved if the following criterion is met:

I. Documentation is provided that there is clinically significant improvement or stabilization in clinical signs and symptoms of disease (including but not limited to reduction in hospitalizations or urgent heart failure visits, improvement or stabilization in 6-Minute Walk Test, improvement in symptom burden or frequency).

Requests for Amvuttra (vutrisiran) may not be approved for the following:

I. Individual has a history of liver or heart transplantation; **OR**
II. Individual has severe renal impairment or end-stage renal disease; **OR**
III. Individual has ~~moderate or~~ severe hepatic impairment; **OR**
~~IV. Individual has New York Heart Association (NYHA) class III or IV heart failure (NCT 03759379); **OR**~~
~~V.~~IV. Individual has sensorimotor or autonomic neuropathy not related to hATTR amyloidosis (including but not limited to, monoclonal gammopathy, autoimmune disease) (NCT 03759379); **OR**
~~VI.~~V. Individual is using in combination with Attruby, Onpattro, Tegsedi, Vyndaqel. Vyndamax, or Wainua; **OR**
~~VII.~~VI. May not be approved when the above criteria are not met and for all other indications.

Quantity Limits

Amvuttra (vutrisiran) Quantity Limit

Drug	Limit
Amvuttra (vutrisiran) 25 mg/0.5 mL syringe	1 syringe per 3 months

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Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS	
J0225	Injection, vutrisiran, 1 mg [Amvuttra]
ICD-10 Diagnosis	
E85.1	Neuropathic heredofamilial amyloidosis
E85.4	Organ-limited amyloidosis [Transthyretin-related (ATTR) familial amyloid cardiomyopathy]

Document History

Revised: 5/16/2025
Document History:

- 5/16/2025 – Select Review: Add approval for new indication for cardiomyopathy. Administrative update to add documentation. Coding Reviewed: Added ICD-10-CM E85.4.
- 8/16/2024 – Annual Review: Add Wainua to may not be used in combination criteria. Coding Reviewed: No changes.
- 8/18/2023 – Annual Review: Wording and formatting changes. Coding Reviewed: No changes.
- 8/19/2022 – Annual Review: No changes. Coding Reviewed: No changes. Effective 1/1/2023 Added HCPCS J0225. Added ICD-10-CM E85.1. Removed HCPCS J3590, J3490.
- 6/13/2022 – Select Review: Add new clinical criteria and quantity limit for Amvuttra. Coding Reviewed: Added HCPCS J3490, J3590. All diagnoses pend.

References

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Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.