Medical Policy

Utilization Management and Clinical Medical Policy

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
vutrisian (Amvuttra®)	MP-RX-FP-193-26	☒ MMM MA ☒ MMM MultiHealth	10/21/2026	10/21/2026
			Last Review Date: 10/21/2026	Frequently Revision: Annual

Service Category:

- ☐ Anesthesia
- ☐ Surgery
- ☐ Radiology Procedures
- ☐ Pathology and Laboratory Procedures
- ☐ Medicine Services and Procedures
- ☐ Evaluation and Management Services
- ☐ DME/Prosthetics or Supplies
- ☒ Other: Part B Drugs

Service Description:

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 (ATTRCM) in adults to reduce cardiovascular mortality, cardiovascular hospitalizations and urgent heart failure visits.

Background Information:

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

Policy Name: vutrisian (Amvuttra®)	Policy Number: MP-RX-FP-193-26	Scope: ☒ MMM MA ☒ MMM MultiHealth	Origination Date: 10/21/2026	Effective Date: 10/21/2026
			Last Review Date: 10/21/2026	Frequently Revision: Annual

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.

Approved Indications

A. For the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.
B. For the treatment of the cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis in adults to reduce cardiovascular mortality, cardiovascular hospitalizations and urgent heart failure visits.

Other Uses

A. None.

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
vutrisian (Amvuttra®)	MP-RX-FP-193-26	☒ MMM MA ☒ MMM MultiHealth	10/21/2026	10/21/2026
			Last Review Date: 10/21/2026	Frequently Revision: Annual

Medical Necessity Guidelines:

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.

vutrisiran (Amvuttra®)

A. Criteria For Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

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).

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.

B. Criteria For Continuation of Therapy

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

Policy Name: vutrisian (Amvuttra®)	Policy Number: MP-RX-FP-193-26	Scope: ☒ MMM MA ☒ MMM MultiHealth	Origination Date: 10/21/2026	Effective Date: 10/21/2026
			Last Review Date: 10/21/2026	Frequently Revision: Annual

i. Individual has a diagnosis of polyneuropathy of hereditary transthyretin (hATTR) amyloidosis; **AND**
ii. Documentation is provided that individual has a TTR mutation verified by genotyping (NCT 03759379); **AND**
iii. 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).

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

C. Authorization Duration

i. Initial Approval Duration: Up to 6 months
ii. Reauthorization Approval Duration: Up to 6 months

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

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

i. Individual has a history of liver or heart transplantation; **OR**
ii. Idividual has sensorimotor or autonomic neuropathy not related to hATTR amyloidosis (including but not limited to, monoclonal gammopathy, autoimmune disease) (NCT 03759379); **OR**
iii. Individual is using in combination with Attruby, Onpattro, Tegsedi, Vyndaqel. Vyndamax, or Wainua; **OR**
iv. May not be approved when the above criteria are not met and for all other indications.

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
vutrisian (Amvuttra®)	MP-RX-FP-193-26	☒ MMM MA ☒ MMM MultiHealth	10/21/2026	10/21/2026
			Last Review Date: 10/21/2026	Frequently Revision: Annual

Limits or Restrictions:

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Drug	Recommended Dosing Schedule	Limit
Amvuttra (vutrisiran) 25 mg/0.5 mL pre-filled syringe	• 25 mg sc every 3 months	1 syringe per 3 months
Exceptions		
• Amvuttra is for subcutaneous use only and should be administered by a healthcare professional.		

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
vutrisian (Amvuttra®)	MP-RX-FP-193-26	☒ MMM MA ☒ MMM MultiHealth	10/21/2026	10/21/2026
			Last Review Date: 10/21/2026	Frequently Revision: Annual

Codes Information:

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

ICD-10 Diagnostic Codes:

Codes	Description
E85.1	Neuropathic heredofamilial amyloidosis [transthyretin-related (ATTR) familial amyloid polyneuropathy]
E85.4	Organ-limited amyloidosis [Transthyretin-related (ATTR) familial amyloid cardiomyopathy]

HCPCS Codes:

Codes	Description
J0225	Injection, vutrisiran, 1 mg [Amvuttra]

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
vutrisian (Amvuttra®)	MP-RX-FP-193-26	☒ MMM MA ☒ MMM MultiHealth	10/21/2026	10/21/2026
			Last Review Date: 10/21/2026	Frequently Revision: Annual

Reference Information:

1. Alnylam Pharmaceuticals, Inc. Amvuttra® (vutrisiran) prescribing information. Revised March 2025. Available at: https://www.alnylam.com/sites/default/files/pdfs/amvuttra-us-prescribing-information.pdf. Accessed August 25, 2026.
2. Alnylam Pharmaceuticals. HELIOS-A: A Study of Vutrisiran (ALN-TTRSC02) in Patients With Hereditary Transthyretin Amyloidosis (hATTR Amyloidosis). NLM Identifier: NCT 03759379. Last updated: June 29, 2025. Available at: https://clinicaltrials.gov/study/NCT03759379?term=NCT03759379&rank=1. Accessed: July 5, 2025.
3. Ando Y, Coelho T, Berk JL, et. al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. Orphanet J Rare Dis. 2013;8(31).
4. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: June 21, 2025.
5. Dorbala S, Ando Y, Bokhari S, et. al. ASNC/AHA/ASE/EANM/HFSA/ISA/SCMR/SNMMI Expert Consensus Recommendations for Multimodality Imaging in Cardiac Amyloidosis: Part 2 of 2-Diagnostic Criteria and Appropriate Utilization. Circ Cardiovasc Imaging. 2021;14:e30.
6. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
7. Fontana M. Cardiac amyloidosis: Treatment and prognosis. Last updated: February 6, 2025. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Accessed: July 2, 2025.
8. Fontana M. Cardiac amyloidosis: Epidemiology, clinical manifestations, and diagnosis. Last updated: May 2, 2024. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Accessed: July 2, 2025.
9. Fontana M, Berk JL, Gillmore JD, et al. Vutrisiran in Patients with Transthyretin Amyloidosis with Cardiomyopathy. N Engl J Med. 2025;392(1):33-44.
10. Gertz MA, Benson MD, Dyck PJ, et. al. Diagnosis, Prognosis, and Therapy of Transthyretin Amyloidosis. J Am Coll Cardiol. 2015;66(21):2451-2466.
11. Heidenreich P, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. J Am Coll Cardiol. 2022 May;79(17):e263–e421.
12. Kittleson M, Ruberg F, 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. JACC. 2023; 81(11):1076–1126.
13. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically

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.

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
vutrisian (Amvuttra®)	MP-RX-FP-193-26	☒ MMM MA ☒ MMM MultiHealth	10/21/2026	10/21/2026
			Last Review Date: 10/21/2026	Frequently Revision: Annual

No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from the health plan.

© CPT Only – American Medical Association

Policy History:

Type of Review	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Policy Inception	Elevance Health's Medical Policy Adoption.	10/15/2026	10/21/2026