DR.025.A AMVUTTRA® (vutrisiran)

Original Implementation Date: 09/08/2026
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Thank you for being a valued provider for members in one or more of our health plans: Jefferson Health Plans Medicare Advantage, Jefferson Health Plans Individual and Family Plans, Jefferson Health Plans CHIP, and/or Jefferson Health Plans EverWell (our Medicaid plan).

***** NOTIFICATION OF PENDING POLICY IMPLEMENTATION *****

Please note that this Policy Bulletin will be implemented on 09/08/2026. This document provides a 30-day notification of its pending implementation and is not currently implemented.

PRODUCT VARIATIONS

This policy applies to all Jefferson Health Plans lines of business unless noted below.

For Medicare Criteria please reference Medicare Step Therapy (Part B criteria)

POLICY STATEMENT

The plan considers AMVUTTRA® (vutrisiran) medically necessary for its FDA approved indications when the prior authorization criteria listed in this policy are met.

FDA APPROVED INDICATIONS

AMVUTTRA® (vutrisiran) is an RNA interference (RNAi) therapeutic that lowers transthyretin (TTR) levels, approved for hereditary transthyretin-mediated amyloidosis and is indicated for the treatment of:

• Polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR-PN) in adults.

• Cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) in adults to reduce cardiovascular mortality, cardiovascular hospitalizations and urgent heart failure visits.

OFF-LABEL USE

N/A

PRIOR AUTHORIZATION CRITERIA

INITIAL CRITERIA:

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

1. The member is 18 years or older **and**

2. Has history of heart failure with at least one prior hospitalization for heart failure (not due to arrythmia or a conduction system disturbance treated with a permanent pacemaker); or has symptoms of heart failure (e.g., dyspnea, edema, volume overload, orthostatic hypotension, syncope, peripheral edema) at baseline; **and**

3. The diagnosis is confirmed by either of the following criteria:

    a. Biopsy proven disease with both:

    - Presence of transthyretin (TTR) amyloid deposits in a tissue biopsy specimen from cardiac or noncardiac origin; **and**

    - Transthyretin precursor proteins presence is confirmed by immunohistochemical analysis, mass spectrometry, tissue staining, or polarized light microscopy.

    b. Technetium-labeled bone scintigraphy proven disease with both:

    - Presence of amyloid deposits; **and**

    - Systemic light chains amyloidosis is ruled out by the absence of monoclonal proteins with all of the following tests-serum kappa/lambda free light chain ratio and serum protein immunofixation and urine protein immunofixation.

c. For members with hereditary ATTR-CM, the diagnosis must also be confirmed with genetic testing (detection of pathogenic or likely pathogenic variants in the TTR gene-Val122Ile variant and Thr60Ala).

4. Diagnostic cardiac imaging (echocardiogram and magnetic imaging) shows heart involvement, such as increased thickness of the ventricular wall or interventricular septum.

5. The medication is prescribed by, or in consultation with, a cardiologist or other healthcare professional specializing in the management of amyloidosis; **and**

6. The member does not have New York Heart Association class IV disease, prior or anticipated heart, liver, or other organ transplant or implantation of left-ventricular assist device; **and**

7. The requested medication will not be used in combination with patisiran (Onpattro), inotersen (Tegsedi), eplontersen (Wainua), acromamidis (Attruby), tafamidis meglumine (Vyndaqel), or tafamidis (Vyndama).

Polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis also known as transthyretin-type familial amyloid polyneuropathy (ATTR-FAP):

1. The member is 18 years older and has a diagnosis of hATTR amyloidosis with polyneuropathy confirmed by molecular genetic testing that reveals pathogenic variation(s) in the transthyretin (TTR) gene; **and**

2. Member exhibits clinical manifestations of ATTR-FAP (e.g., amyloid deposition in biopsy specimens, TTR protein variants in serum, progressive peripheral sensory-motor polyneuropathy); **and**

3. Member is not a liver transplant recipient; **and**

4. The medication is prescribed by or in consultation with a neurologist, geneticist, or healthcare professional specializing in the treatment of amyloidosis; **and**

5. The requested medication will not be used in combination with patisiran (Onpattro), inotersen (Tegsedi), eplontersen (Wainua), acromamidis (Attruby), tafamidis meglumine (Vyndaqel), or tafamidis (Vyndamax); **and**

Authorization duration is limited to no more than 12 months.

RENEWAL CRITERIA

1. The member has previously received treatment with Amvuttra.

2. For cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM):

    a. Member has met all initial authorization criteria;

    b. Member has demonstrated a beneficial response to treatment with the requested medication compared to baseline (e.g., improvement in rate of disease progression as demonstrated by distance walked on the 6-minute walk test, the Kansas City Cardiomyopathy Questionnaire-Overall Summary [KCCQ-OS] score, cardiovascular-related hospitalizations, New York Heart Association [NYHA] classification of heart failure, left ventricular stroke volume, N-terminal B-type natriuretic peptide [NT-proBNP] level).

3. For polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR-PN):

    a. Member has met all initial authorization criteria;

    b. Member has demonstrated a beneficial response to treatment with the requested medication compared to baseline (e.g., improvement of neuropathy severity and rate of disease progression as demonstrated by the modified Neuropathy Impairment Scale+7 [mNIS+7] composite score, the Norfolk Quality of Life-Diabetic Neuropathy [QoL-DN] total score, polyneuropathy disability [PND] score, FAP disease stage, manual grip strength).

The member is not receiving Amvuttra in combination with any of the following:

- RNA interference agents (e.g., Onpattro, Wainua, Tegsedi); or
- Transthyretin stabilizers (e.g., Vyndaqel or Vyndamax); and
- Authorization duration is limited to no more than 12 months.

DOSAGE AND ADMINISTRATION

See package labeling.

RISK FACTORS/SIDE EFFECTS

See package labeling.

MONITORING

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 the recommended daily allowance of vitamin A should not be given to try to achieve normal serum vitamin A levels during treatment, 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, vision changes, dry eyes).

CONTRAINDICATIONS

N/A

BLACK BOX WARNING

N/A

CLINICAL EVIDENCE

The efficacy of AMVUTTRA® (vutrisiran) has been demonstrated in randomized, controlled clinical trials across both approved indications: polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR-PN) and cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM).

hATTR Amyloidosis with Polyneuropathy

Efficacy in adults with hATTR-PN was evaluated in the **HELIOS-A trial**, a randomized, open-label, active-controlled study comparing vutrisiran with patisiran. Treatment with AMVUTTRA resulted in statistically significant and clinically meaningful improvements in neuropathy impairment, as measured by the modified Neuropathy Impairment Score +7 (mNIS+7), compared with baseline. Patients treated with vutrisiran also demonstrated improvements or stabilization in health-related quality-of-life outcomes, including results from the Norfolk

Quality of Life–Diabetic Neuropathy (Norfolk QOL-DN) questionnaire. These findings support the ability of AMVUTTRA to slow disease progression and improve neurologic outcomes in adults with hATTR-PN.

ATTR Amyloidosis with Cardiomyopathy

Efficacy in adults with ATTR-CM was demonstrated in the **HELIOS-B trial**, a randomized, double-blind, placebo-controlled study that enrolled patients with wild-type or hereditary ATTR amyloidosis with cardiomyopathy. Treatment with AMVUTTRA led to a statistically significant reduction in the composite endpoint of cardiovascular mortality, cardiovascular hospitalizations, and urgent heart failure visits compared with placebo. Additional benefits were observed in measures of functional capacity and health-related quality of life. These results supported the FDA approval of AMVUTTRA for the treatment of ATTR-CM in March 2025.

Clinical Relevance

Across both neurologic and cardiac manifestations of ATTR amyloidosis, AMVUTTRA®has demonstrated clinically meaningful efficacy by reducing circulating transthyretin (TTR) levels and thereby addressing the underlying cause of amyloid deposition. The observed improvements in disease-specific clinical outcomes and major cardiovascular events support AMVUTTRA as a disease-modifying therapy for a broad adult ATTR patient population.

BACKGROUND

AMVUTTRA® (vutrisiran) is an RNA interference (RNAi) therapeutic developed for the treatment of transthyretin-mediated amyloidosis (ATTR amyloidosis), a rare, progressive, and potentially life-threatening condition caused by the misfolding and accumulation of transthyretin (TTR) protein in tissues. ATTR amyloidosis may be hereditary (hATTR), resulting from pathogenic variants in the TTR gene, or wild-type (wtATTR), which occurs in the absence of genetic mutations and primarily affects older adults. Vutrisiran is a transthyretin-directed small interfering RNA that targets hepatic production of both mutant and wild-type TTR, leading to marked reductions in circulating TTR levels and addressing the underlying source of amyloid formation. AMVUTTRA® was initially approved by the U.S. Food and Drug Administration (FDA) in 2022 for the treatment of polyneuropathy of hereditary ATTR amyloidosis in adults and received an expanded FDA approval in March 2025 for the treatment of cardiomyopathy of wild-type or

hereditary ATTR amyloidosis in adults to reduce cardiovascular mortality, cardiovascular hospitalizations, and urgent heart failure visits.

CODING

Note: *The Current Procedural Terminology (CPT®), Healthcare Common Procedure Coding System (HCPCS), and the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) codes that may be listed in this policy are for reference purposes only. Listing of a code in this policy does not imply that the service is covered and is not a guarantee of payment. Other policies and coverage guidelines may apply. When reporting services, providers/facilities should code to the highest level of specificity using the code that was in effect on the date the service was rendered. This list may not be all inclusive.*

CPT® is a registered trademark of the American Medical Association.

CPT Code	Description
N/A	

HCPCS Code	Description
J0225	Injection, vutrisiran, 1 mg

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

DISCLAIMER

Approval or denial of payment does not constitute medical advice and is neither intended to guide nor influence medical decision making. Policy Bulletins are developed to assist in administering plan benefits and constitute neither offers of

coverage nor medical advice. This Policy Bulletin may be updated and therefore is subject to change.

For Jefferson Health Plans EverWell and Jefferson Health Plans CHIP products any requests for services that do not meet criteria set in PARP will be evaluated on a case-by-case basis.

POLICY HISTORY

This section provides a high-level summary of changes to the policy since the previous version.

Summary	Version	Version Date
New policy.	A	09/08/2026

REFERENCES

1. Amvuttra® (Vutrisiran) package insert: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/215515s006lbl.pdf

2. Safety: https://www.amvuttrahcp.com/safety-profile

3. Transthyretin Amyloid Polyneuropathy (ATTR-PN): https://www.rarediseaseadvisor.com/disease-info-pages/transthyretin-amyloid-polyneuropathy-guidelines/

4. JAMA : https://jamanetwork.com/journals/jama/fullarticle/2794781

5. Amvuttra®: https://www.amvuttrahcp.com/

6. Alnylam announces FDA approval of AMVUTTRA® (vutrisiran), the First RNAi Therapeutic to Reduce Cardiovascular Death, Hospitalizations and Urgent Heart Failure Visits in Adults with ATTR Amyloidosis with Cardiomyopathy (ATTR-CM): https://investors.alnylam.com/press-release?id=28831

7. DailyMed (National Library of Medicine): https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=8db0facb-81b6-4006-9239-27dc6409c5d3

8. Overview of amyloidosis, Peter D Goevic, MD, UpToDate -last update: Apr 10, 2026

9. Cardiac amyloidosis: Treatment and prognosis, Marianna Fontana, MD, UpToDate-last update: Feb 03, 2026

10. Neurologic manifestations and management of systemic amyloidosis, Long Davalos, MD Mazen M Dimachkie, MD, UpToDate-last update: May 08, 2026