amvuttra® (vutrisiran) injection 25 mg/0.5 mL

FOR YOUR PATIENTS WITH CARDIOMYOPATHY OF TRANSTHYRETIN-MEDIATED AMYLOIDOSIS OR WITH POLYNEUROPATHY OF HEREDITARY TRANSTHYRETIN-MEDIATED AMYLOIDOSIS

Choose AMVUTTRA® (vutrisiran)— **the first and only silencer for both ATTR-CM & hATTR-PN**[1-4]

See how AMVUTTRA could be an appropriate first choice for your patients with ATTR-CM or hATTR-PN[4,5]

ATTR-CM=cardiomyopathy of transthyretin-mediated amyloidosis; hATTR-PN=polyneuropathy of hereditary transthyretin-mediated amyloidosis.

Indications

AMVUTTRA® (vutrisiran) is indicated for the 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.
- polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR-PN) in adults.

Important Safety Information

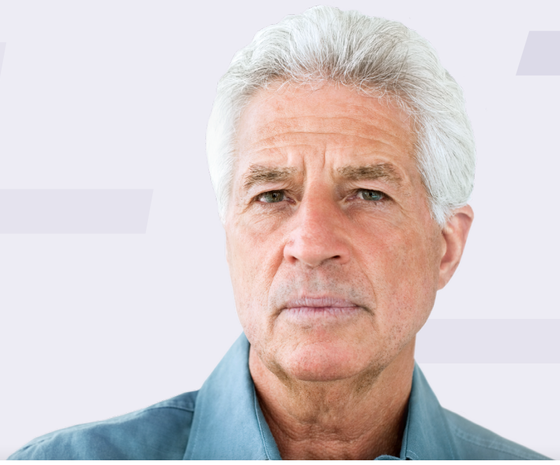
Reduced Serum Vitamin A Levels and Recommended Supplementation

AMVUTTRA treatment leads to a decrease in serum vitamin A levels.

Supplementation at the recommended daily allowance (RDA) of vitamin A is advised for patients taking AMVUTTRA. Higher doses than the RDA 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).

Please see additional Important Safety Information on next page and full Prescribing Information.



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Recently diagnosed with wtATTR-CM

GENE, 66

Not an actual patient.

Gene is concerned about the challenges posed by his recent diagnosis of ATTR-CM and wants to be able to travel, stay involved with his family, and continue playing golf.

Choose AMVUTTRA first—
for patients like Gene who have been recently diagnosed with ATTR-CM.

Medical History

- Recently diagnosed with wtATTR-CM
- NYHA class I
- Hypertension

Results of Clinical Assessments[6-10]

- Low QRS voltage on ECG
- Echocardiogram: LV wall thickness of 13 mm (normal range ≤12 mm)
- NT-proBNP level increased from 592 pg/mL to 763 pg/mL in the last 12 months (normal range <125 pg/mL)

Current Medications[10]*

- ACE inhibitor

Insurance

- Medicare FFS

*Patient may be on additional medications for other comorbidities.

ACE=angiotensin-converting enzyme; ATTR-CM=cardiomyopathy of transthyretin-mediated amyloidosis; ECG=electrocardiogram; FFS=fee for service; LV=left ventricular; NT-proBNP=N-terminal prohormone of brain-type natriuretic peptide; NYHA=New York Heart Association; wtATTR-CM=cardiomyopathy of wild-type transthyretin-mediated amyloidosis.

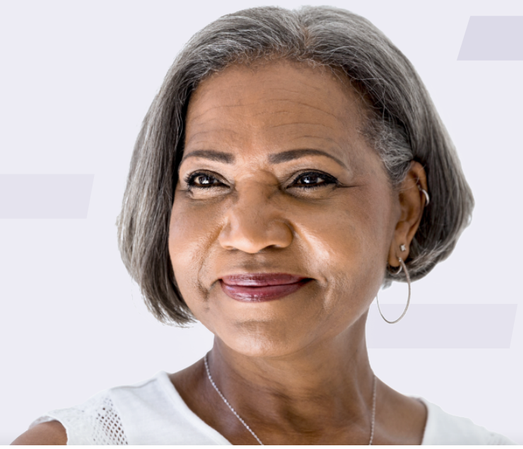
Important Safety Information

Adverse Reactions

In a study of patients with hATTR-PN, the most common adverse reactions that occurred in patients treated with AMVUTTRA were pain in extremity (15%), arthralgia (11%), dyspnea (7%), and vitamin A decreased (7%).

In a study of patients with ATTR-CM, no new safety issues were identified.

Please see additional Important Safety Information on the front cover and full Prescribing Information.



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hATTR, V122I, mixed phenotype

DIANE, 67

Not an actual patient.

Diane is discouraged by her declining health and journey to the correct diagnosis of hATTR. She worries that she is a burden to others, but she is motivated to treat her hATTR and slow progression.

Prescribe AMVUTTRA—
the first and only therapy approved to treat both the polyneuropathy and cardiomyopathy of hereditary ATTR.[1]

Medical History[4,6,7,11]

- Diagnosed a few months ago with hATTR with V122I variant
- Symptoms include:
  - Fatigue, dyspnea on exertion consistent with CM manifestations
  - Numbness/tingling in upper and lower extremities consistent with PN manifestations
- NYHA class II
- Carpal tunnel syndrome
- Atrial fibrillation
- Diabetes

Results of Clinical Assessments[6-10,12]

- Echocardiogram: LV ejection fraction 48%, LV wall thickness at 14 mm (normal range ≤12 mm)
- NT-proBNP level increased from 1150 pg/mL to 1500 pg/mL in 12 months (normal range <125 pg/mL)

Current Medications[7,10-12]*

- ACE inhibitor, anticoagulant, metformin, loop diuretic

Insurance

- Commercial insurance

*Patient may be on additional medications for other comorbidities.

ACE=angiotensin-converting enzyme; ATTR=transthyretin-mediated amyloidosis; CM=cardiomyopathy; hATTR=hereditary transthyretin-mediated amyloidosis; LV=left ventricular; NT-proBNP=N-terminal prohormone of brain-type natriuretic peptide; NYHA=New York Heart Association; PN=polyneuropathy; V122I=valine-to-isoleucine substitution at position 122.

Select Important Safety Information

Reduced Serum Vitamin A Levels and Recommended Supplementation
AMVUTTRA treatment leads to a decrease in serum vitamin A levels.
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Patients should be referred to an ophthalmologist if they develop ocular symptoms suggestive of vitamin A deficiency (e.g., night blindness).

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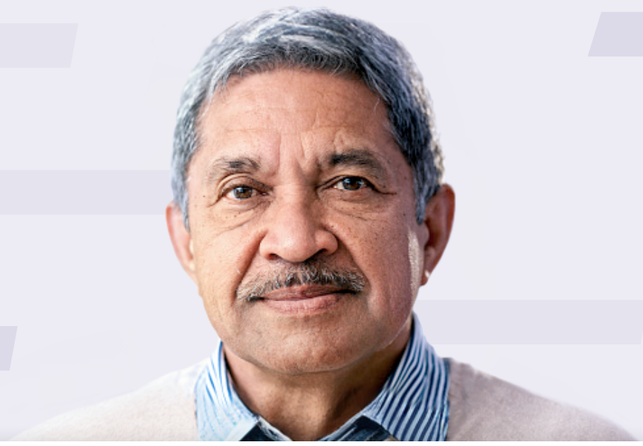

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NYHA class III with wtATTR-CM

RICHARD, 75

Not an actual patient.

Richard's independence is rapidly diminishing, and he finds himself increasingly socially isolated. He hopes to attend his granddaughter's upcoming wedding, and despite struggling with compliance on his current medications, Richard is willing to follow what his doctor recommends to treat his ATTR-CM.

Prescribe AMVUTTRA—
for confidence in monitoring patient compliance with HCP-administered doses only 4 times per year.[1]*

Medical History

- Diagnosed with wtATTR-CM 1 year ago
- Symptoms include[6,11-13]:
  - Dyspnea, fatigue, swelling in lower extremities
  - Muscular weakness, chronic constipation, pain in joints and tendons
- NYHA class III
- Atrial fibrillation

Results of Clinical Assessments[6-10,14,15]

- Echocardiogram: LV ejection fraction of 40%, LV wall thickness of 18 mm (normal range ≤12 mm)
- NT-proBNP level 3000 pg/mL
- eGFR of 60 mL/min/1.73 m^2

Current Medications[9,10†]

- ACE inhibitor, anticoagulant, beta-blocker, loop diuretic

Insurance

- Medicare Advantage

*AMVUTTRA is administered every 3 months.
†Patient may be on additional medications for other comorbidities.

ACE=angiotensin-converting enzyme; ATTR-CM=cardiomyopathy of transthyretin-mediated amyloidosis; eGFR=estimated glomerular filtration rate; HCP=healthcare professional; LV=left ventricular; NT-proBNP=N-terminal prohormone of brain-type natriuretic peptide; NYHA=New York Heart Association; wtATTR-CM=cardiomyopathy of wild-type transthyretin-mediated amyloidosis.

Important Safety Information

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In a study of patients with hATTR-PN, the most common adverse reactions that occurred in patients treated with AMVUTTRA were pain in extremity (15%), arthralgia (11%), dyspnea (7%), and vitamin A decreased (7%).

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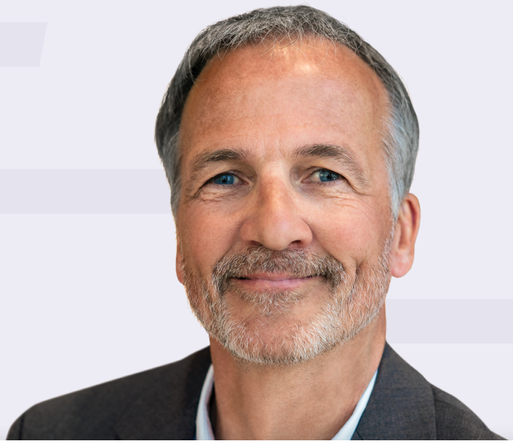

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hATTR-PN, V30M, with new-onset polyneuropathy symptoms

STEVEN, 58

Not an actual patient.

Steven has sensory and motor neuropathy that began in his feet and has recently moved up his legs, affecting his ability to walk. He has also had a decline in grip strength, which has recently made everyday tasks more challenging. Recurrent nausea and diarrhea have led to unintentional weight loss, limiting his socialization with family and friends.

Prescribe AMVUTTRA—
the #1 prescribed treatment for the polyneuropathy of hATTR in adults.[16]

Medical History[17-19]

- Bilateral carpal tunnel syndrome
- Persistent GI issues (nausea/diarrhea)
- Prior misdiagnosis of idiopathic polyneuropathy

Results of Clinical Assessments[11,17,19,20]

- Nerve conduction: Axonal polyneuropathy and slowed median nerve conduction velocity across carpal tunnel
- sFLC test: Monoclonal light chains not present
- Genetic testing confirmed TTR variant

Current Medications[21]*

- Gabapentin

Insurance

- Commercial

*Patient may be on additional medications for other comorbidities.

GI=gastrointestinal; hATTR=hereditary transthyretin-mediated amyloidosis; hATTR-PN=polyneuropathy of transthyretin-mediated amyloidosis; sFLC=serum free light-chain; TTR=transthyretin; V30M=valine-to-methionine substitution at position 30.

Select Important Safety Information

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AMVUTTRA treatment leads to a decrease in serum vitamin A levels.
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Patient Profiles Summary

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Recently diagnosed with wtATTR-CM

Choose AMVUTTRA first— for patients like Gene who have been recently diagnosed with ATTR-CM.

DIANE, 67

hATTR, V122I, mixed phenotype

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RICHARD, 75

NYHA class III with wtATTR-CM

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STEVEN, 58

hATTR-PN, V30M, with new-onset polyneuropathy symptoms

Prescribe AMVUTTRA— the #1 prescribed treatment for the polyneuropathy of hATTR in adults.[16]

Learn how AMVUTTRA could be an appropriate first choice for your patients with ATTR-CM & hATTR-PN.[4,5]

For more information, visit **www.amvuttrahcp.com**

Please see Indications on front cover and Important Safety Information throughout, including reduced serum vitamin A levels and recommended supplementation, and full Prescribing Information.

References: 1. AMVUTTRA Prescribing Information. Cambridge, MA: Alnylam Pharmaceuticals, Inc. **2.** Tomasoni et al. *Front Cardiovasc Med.* 2023;10:1154594. **3.** Williams et al. *J Cardiothorac Vasc Anesth.* 2024;38(7):1457-1459. **4.** Fontana et al. *N Engl J Med.* 2025;392(1):33-44. **5.** Adams et al. *Amyloid*. 2023;30(1):18-26. **6.** Maurer et al. *Circ Heart Fail.* 2019;12(9):e006075. **7.** Mohty et al. *Arch Cardiovasc Dis.* 2013;106(10):528–540. **8.** Heidenreich et al. *Circulation.* 2022;145(18):e895-e1032. **9.** Moya et al. *ESC Heart Fail.* 2023;10(6):3483–3492. **10.** Witteles et al. *JACC Heart Fail.* 2019;7(8):709-716. **11.** Kittleson et al. *J Am Coll Cardiol.* 2020;81(11):1076-1126. **12.** Patel et al. *Eur J Heart Fail.* 2022;24(12):2355-2363. **13.** Perfetto et al. *Biomedicines.* 2022;10(12):3226. **14.** Alonso et al. *ESC Heart Fail.* 2024;11(6):3649–3655. **15.** Delanaye et al. *Clin Biochem Rev.* 2016;37(1):17-26. **16.** Data on file. Alnylam Pharmaceuticals, Inc. **17.** Kittleson et al. *J Am Coll Cardiol*. 2023;81(11):1076-1126. **18.** Adams et al. *J Neurol*. 2021;268(6):2109-2122. **19.** Hawkins et al. *Ann Med.* 2015;47(8):625-638. **20.** Escolano-Lazano et al. *J Clin Neurol*. 2024;20(6):610-616. **21.** Gabapentin Prescribing Information. Actavis Pharma, Inc.

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Alnylam® PHARMACEUTICALS