Patients with the polyneuropathy of hATTR amyloidosis face progressively worsening symptoms[1-3]; no patient should go without appropriate treatment

hATTR=hereditary transthyretin-mediated.

Indication and Important Safety Information

Indication

AMVUTTRA is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis 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).

Adverse Reactions

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%).

Please see Important Safety Information throughout and full Prescribing Information.

amvuttra® (vutrisiran) injection 25 mg/0.5 mL

amvuttra (vutrisiran) injection 25 mg/0.5 mL

Marcus is concerned about the cost of another medication

***Patient profiles and photos are not of actual patients.**

Patient health concerns[1,4,6-10]:

- Already on a daily regimen of multiple medications that includes one for cardiac complications related to hATTR amyloidosis
- Pain and tingling in his hands and feet are making daily tasks such as showering and navigating stairs challenging
- Experiencing erectile dysfunction due to autonomic neuropathy

Patient lifestyle

- Staying adherent to multiple medications is vital to Marcus given his disease burden, but he is concerned about adding a treatment for his polyneuropathy of hATTR amyloidosis due to out-of-pocket costs

Four-times-a-year AMVUTTRA® is accessible and affordable for most patients regardless of insurance type[a]

- [More than 65% of patients have no out-of-pocket costs for AMVUTTRA][b]
- For many patients with Medicare, AMVUTTRA is covered under the medical benefit and not the pharmacy benefit
- The majority of patients with Medicare FFS have supplemental coverage that reduces their cost-sharing obligation

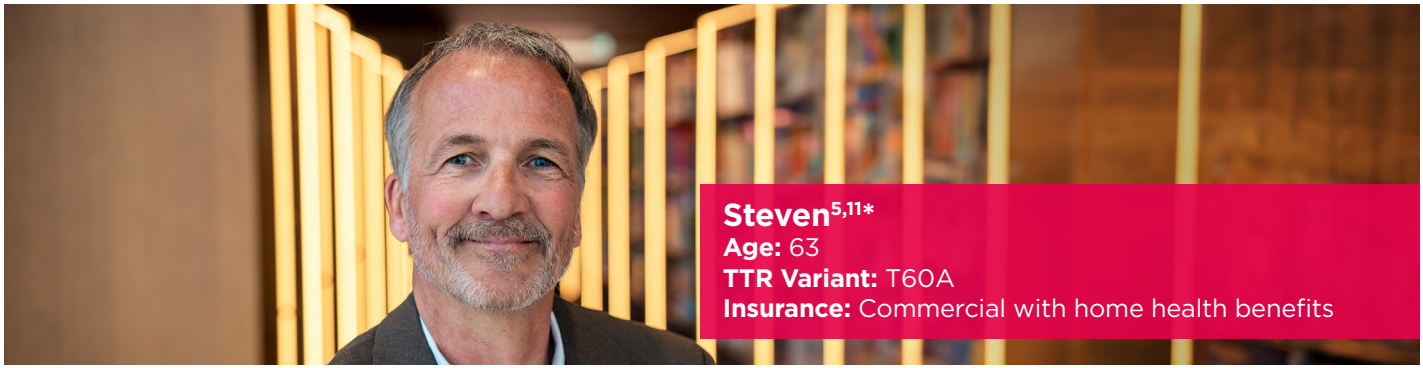
[a]Administered once every 3 months by a healthcare professional.
[b]As of [date].

FFS=Fee-for-Service.

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

amvuttra (vutrisiran) injection 25 mg/0.5 mL

Steven struggles with new-onset polyneuropathy symptoms that interrupt his daily activities



***Patient profiles and photos are not of actual patients.**

Patient health concerns[1,6,9,12,13]:

- Is noticing new polyneuropathy symptoms, including a decline in grip strength that makes everyday tasks more challenging
- Taking more breaks than usual during morning walks due to fatigue

Patient lifestyle

- Continuing his routine morning walks and cheering on his grandchildren at their soccer games is important to Steven

AMVUTTRA® offers you and your patients the flexibility to decide the best place to receive treatment

- >[50%] of patients enrolled in Alnylam Assist® have a home health benefit through their insurance, allowing them to receive HCP-administered AMVUTTRA 4 times a year[a] in the comfort of their own home
- Alnylam Assist can help investigate your patient's insurance benefits and answer questions about home administration

[a]Administered once every 3 months.

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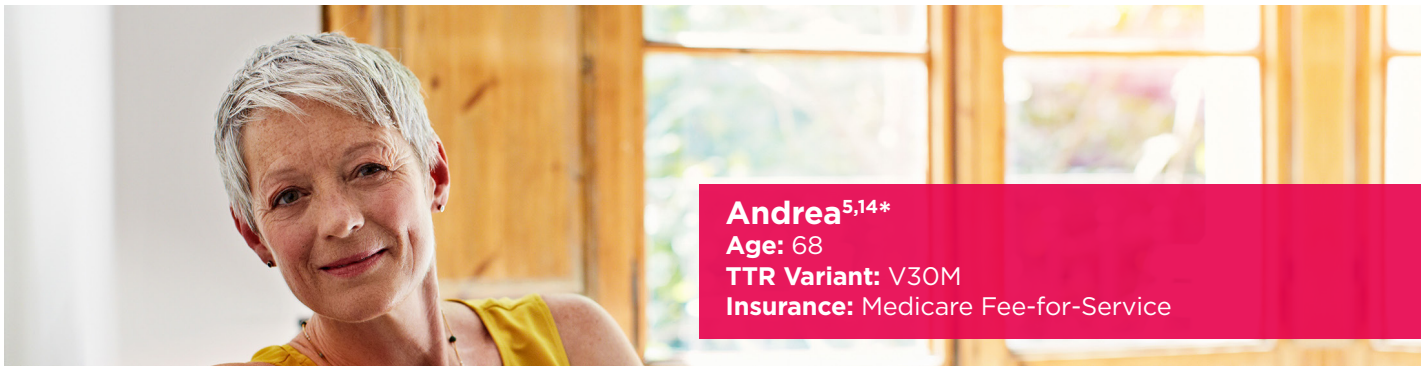
Andrea prefers less frequent injections



***Patient profiles and photos are not of actual patients.**

Patient health concerns[1,6,9,10,12,13]:

- Sensory and motor neuropathy that began in the lower extremities has started to spread to her upper limbs
- Recurrent nausea and diarrhea have led to unintentional weight loss, limiting socialization with family and friends

Patient lifestyle

- Andrea has limited caregiver support

AMVUTTRA® requires the fewest doses to treat the polyneuropathy of hATTR amyloidosis[15-18]

- AMVUTTRA is HCP-administered 4 times a year,[a] providing the opportunity for consistent touchpoints in your patients' healthcare routine[15]
- HCP administration helps ensure confidence that each dose is administered fully and properly, without the need for premedication or laboratory monitoring[1]

[a]Administered once every 3 months.

Important Safety Information

Adverse Reactions

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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amvuttra (vutrisiran) injection 25 mg/0.5 mL

Eric asks for an AMVUTTRA® treatment site closer to home

***Patient profiles and photos are not of actual patients.**

Patient health concerns[1,9,10,20]:

- Has difficulty walking due to pain and numbness in feet
- Had a minor fall recently due to orthostatic hypotension and dizziness, and is concerned about falling again

Patient lifestyle

- Has caregiver drive him to his neurologist's office two hours away for his injection, but would like to cut down on travel

You and your patients have the flexibility to decide the best place to receive treatment—whether in your office, at a local clinic (one of the [>900] in the Alnylam Treatment Center Directory), or in the patient's home[a]

- AMVUTTRA is dosed 4 times a year[b] via subcutaneous injection, without the need for premedication or laboratory monitoring[15]
- Alnylam Assist® offers support services to help your patients access AMVUTTRA upon receipt of the Start Form. Contact an Alnylam Case Manager at 1-833-256-2748 from Monday–Friday, 8AM–6PM

[a]If covered by patient's insurance.
[b]Administered once every 3 months by a healthcare professional.

References: 1. Ando Y, Coelho T, Berk JL, et al. *Orphanet J Rare Dis*. 2013;8:31. **2.** Adams D, Coelho T, Obici L, et al. *Neurology*. 2015;85(8):675-682. **3.** Swiecicki PL, Zhen DB, Mauermann ML, et al. *Amyloid*. 2015;22(2):123-131. **4.** Parker MM, Damrauer SM, Tcheandjieu C, et al. *Sci Rep*. 2021;11(1):11645. **5.** Maurer MS, Hanna M, Grogan M, et al. *J Am Coll Cardiol*. 2016;68(2):161-172. **6.** Wixner J, Mundayat R, Karayal ON, et al. *Orphanet J Rare Dis*. 2014;9:61. **7.** Hawkins PN, Ando Y, Dispenzieri A, et al. *Ann Med*. 2015;47(8):625-638. **8.** Adams D, Suhr OB, Hund E, et al. *Curr Opin Neurol*. 2016;29(suppl 1):S14-S26. **9.** Lovley A, Raymond K, Guthrie SD, Pollock M, Sanchorawala V, White MK. *J Patient Rep Outcomes*. 2021;5(1):3. **10.** Gendre T, Planté-Bordeneuve V. *Clin Auton Res* 2019;29(suppl 1):S25-S31. **11.** Reilly MM, Staunton H, Harding AE. *J Neurol Neurosurg Psych*. 1995;59(1):45-49. **12.** Adams D, Algalarrondo V, Polydefkis M, et al. *Orphanet J Rare Dis*. 2021;16(411):1-17. **13.** Rintell D, Heath D, Braga Mendendez F, et al. *Orphanet J Rare Dis*. 2021;16(70):1-13. **14.** Gentile L, Coelho T, Dispenzieri A, et al. *Orphanet J Rare Dis*. 2023;18(350):1-12. **15.** AMVUTTRA Prescribing Information. Cambridge, MA: Alnylam Pharmaceuticals, Inc. **16.** ONPATTRO Prescribing Information. Cambridge, MA: Alnylam Pharmaceuticals, Inc. **17.** TEGSEDI Prescribing Information. Waltham, MA: Akcea Therapeutics, Inc. **18.** WAINUA Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP. **19.** Waddington-Cruz M, Schmidt H, Botteman MF, et al. *Orphanet J Rare Dis*. 2019;14(34):1-7. **20.** González-Duarte A, Barroso F, Mundayat R, et al. *Auton Neurosci*. 2019;222:102590. **21.** Adams D, Tournev IL, Taylor MS, et al. *Amyloid*. 2023;30(1):1-9. **22.** Data on file. Alnylam Pharmaceuticals, Inc.

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

For adult patients with the polyneuropathy of hATTR amyloidosis

AMVUTTRA® (vutrisiran) is the only treatment that can reverse the polyneuropathy manifestations of hATTR amyloidosis with 4 doses per year[15-18,21,a,b]

- In the HELIOS-A trial, treatment with AMVUTTRA led to rapid knockdown of TTR as early as 3 weeks. AMVUTTRA is the only FDA-approved TTR-lowering agent to achieve a mean TTR knockdown level as high as 88% over 18 months[15-18,21]
- At 9 months in the randomized, open-label study, patients treated with AMVUTTRA were compared with an external placebo group and demonstrated:
  - Improvement in neuropathy impairment, as measured by mNIS+7[15]
  - Improvement in quality of life, as measured by the Norfolk QoL-DN[15]
  - Improvement in gait speed, as measured by 10-meter walk test[15]
- The most common adverse reactions were pain in extremity, arthralgia, dyspnea, and vitamin A decreased[15]
- More than [1,000] patients are receiving treatment with AMVUTTRA in the US, making it the #1 prescribed treatment for the polyneuropathy of hATTR amyloidosis in adults[22]
- Four-times-a-year[a] AMVUTTRA is accessible and affordable for most patients, regardless of insurance type

[a]Administered once every 3 months by a healthcare professional.
[b]48% of patients treated with AMVUTTRA experienced reversal in neuropathy impairment from baseline vs. 4% of patients in external placebo group at 18 months.

Find more information about AMVUTTRA for your patients at www.amvuttrahcp.com

mNIS+7=modified Neuropathy Impairment Score + 7; Norfolk QoL-DN=Norfolk Quality of Life-Diabetic Neuropathy; TTR=transthyretin.

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Alnylam® PHARMACEUTICALS

AMV-USA-00777

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