

# AMVUTTRA® (vutrisiran)

## Product Fact Sheet

- AMVUTTRA is approved by the U.S. Food and Drug Administration (FDA) for the treatment of the polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis in adults.
- hATTR amyloidosis is a rare, inherited, rapidly progressive, debilitating and fatal disease caused by a variant, or change, in the transthyretin (TTR) gene that results in misfolded TTR protein accumulating as amyloid deposits in multiple organs and tissues including the nerves, heart and gastrointestinal tract.<sup>1,2</sup>
- The buildup of amyloid deposits throughout the body can result in frequent and early polyneuropathy symptoms, including sensory-motor neuropathy, autonomic neuropathy and gastrointestinal manifestations.<sup>3,4</sup>
- AMVUTTRA is an RNAi (RNA interference) therapeutic that harnesses the body's natural process to silence TTR messenger RNA and reduce the production of TTR protein in the liver, which helps to decrease the amount of amyloid deposits. The decrease in amyloid deposits may result in fewer polyneuropathy symptoms.<sup>5</sup>
- AMVUTTRA uses an Enhanced Stabilization Chemistry-GalNAc conjugate, designed for high metabolic stability, resulting in increased potency and prolonged duration of activity to allow infrequent dosing.<sup>6</sup>
- AMVUTTRA is a subcutaneous injection administered by a healthcare professional once every three months.
- The efficacy and safety of AMVUTTRA were evaluated in the 18-month HELIOS-A Phase 3 trial of 164 adult patients with polyneuropathy caused by hATTR amyloidosis, where AMVUTTRA met all primary and secondary endpoints at 9 months.<sup>5</sup>
  - AMVUTTRA-treated patients showed significant improvement in nerve function and quality of life at 9 months and continued to improve throughout the study, compared with those who received placebo in a similar study.<sup>5</sup>
  - AMVUTTRA also improved other key measures of disease burden relative to external placebo.<sup>5</sup>
- AMVUTTRA demonstrated an encouraging safety and tolerability profile through 18 months of treatment.<sup>5</sup>
  - The most common adverse reactions were pain in extremity, arthralgia, dyspnea and vitamin A decreased.
- For more information about AMVUTTRA, please visit [AMVUTTRA.com](http://AMVUTTRA.com).

Please see Important Safety Information and access full Prescribing Information for AMVUTTRA on page 3.

## AMVUTTRA® Clinical Profile at a Glance<sup>5</sup>

- The efficacy and safety of AMVUTTRA were evaluated in the global, randomized, open-label, multicenter Phase 3 HELIOS-A study across a diverse group of adult patients with hATTR amyloidosis with polyneuropathy. The efficacy of AMVUTTRA was assessed by comparing the AMVUTTRA group in HELIOS-A with those who received placebo in a similar study.
  - AMVUTTRA met the primary endpoint at 9 months, significantly improving nerve function, while patients who received placebo got worse. At 18 months:
    - 48% of AMVUTTRA-treated patients regained some nerve function from the start of treatment compared with 4% of those who received placebo.
      - For the patients who received AMVUTTRA and did not regain some nerve function, progression of their neuropathy was slowed compared with those who received placebo.
    - Nerve function was assessed using a scale called the modified Neuropathy Impairment Score + 7 (mNIS+7) that measured strength and sensation in the hands, feet, arms, and legs; reflexes; and blood pressure upon standing.<sup>i</sup>
  - AMVUTTRA met all secondary endpoints at 9 months, significantly improving quality of life and improving other key measures of disease burden.
    - At 18 months, 57% of AMVUTTRA-treated patients reported better quality of life from the start of treatment, compared with 10% of those who received placebo, as assessed by the Norfolk Quality of Life Diabetic Neuropathy (Norfolk QoL-DN) questionnaire, which asked patients about the severity of their polyneuropathy symptoms, how often they experienced them, and what impact they felt they had on their daily lives.<sup>ii</sup>
    - AMVUTTRA-treated patients also maintained a better walking speed<sup>iii</sup>, experienced improvement in nutritional health<sup>iv</sup> and were better able to perform common daily activities at 18 months compared with placebo-treated patients.<sup>v</sup>
  - Treatment with AMVUTTRA led to rapid, powerful, and sustained reduction in serum TTR, with an 88% mean reduction of serum TTR with dosing once every 3 months.
- AMVUTTRA reduces serum vitamin A levels. Patients should take the recommended daily allowance of vitamin A, and tell their physician if they experience symptoms suggestive of vitamin A deficiency (e.g., night blindness).

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<sup>i</sup> Higher scores indicate more severe disease (total score ranges from 0 to 304).

<sup>ii</sup> Higher scores indicate more severe impact of polyneuropathy symptoms on daily life (total score ranges from -4 to 136).

<sup>iii</sup> Evaluated using the 10-meter walk test, a stopwatch-timed measure of a patient's walking speed over 10 meters.

<sup>iv</sup> Evaluated using modified body mass index, an assessment of height, weight, and the balance of fluids in the body.

<sup>v</sup> Assessed using a 24-item questionnaire called R-ODS, in which patients rated their ability to complete tasks at the beginning of the study and at the end of the study.

## About RNAi Therapeutics

- RNAi (RNA interference) is a natural cellular process of gene silencing that represents one of the most promising and rapidly advancing frontiers in biology and drug development today.<sup>7</sup> This discovery was recognized with the award of the 2006 Nobel Prize for Physiology or Medicine.<sup>8</sup>
- By harnessing the natural biological process of RNAi occurring in our cells, a new class of medicines, known as RNAi therapeutics, is now a reality. Small interfering RNA (siRNA), the molecules that mediate RNAi and comprise Alnylam's RNAi therapeutic platform, function by silencing messenger RNA (mRNA) – the genetic precursors – that encode for disease-causing proteins, thus reducing their production.<sup>7</sup>

## Access to AMVUTTRA® (vutrisiran): Alnylam Assist®

The Alnylam Assist program offers support to patients throughout their treatment with AMVUTTRA, including helping patients understand their insurance coverage and options for financial support based on eligibility. An Alnylam Case Manager will work with a patient to begin treatment with and maintain access to AMVUTTRA. An Alnylam Patient Education Liaison can provide education to help patients and their family members better understand the disease and answer questions about AMVUTTRA. Learn more about Alnylam Assist by visiting [AlnylamAssist.com/AMVUTTRA](https://AlnylamAssist.com/AMVUTTRA).

## 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%).

For additional information about AMVUTTRA, please see the full [Prescribing Information](#).

<sup>1</sup> Hanna M. *Curr Heart Fail Rep*. 2014;11:50-57.

<sup>2</sup> Mohty D, Damy T, Pierre C, et al. *Arch Cardiovasc Dis*. 2013;106:528-540.

<sup>3</sup> Adams D, Coelho T, Obici L, et al. *Neurology*. 2015;85:675-682.

<sup>4</sup> Conceição I, González-Duarte A, Obici L, et al. *J Peripher Nerv Syst*. 2016;21(1):5-9.

<sup>5</sup> Adams D, Tournev IL, Taylor MS, et al. *Amyloid*. 2023;30(1):18-26.

<sup>6</sup> Nair JK, Attarwala H, Seghal A, et al. *Nucleic Acids Res*. 2017;45(19):10969-10977.

<sup>7</sup> Elbashir SM, Harborth J, Lendeckel W, Yalcin A, Weber K, Tuschl T. *Nature*. 2001;411:494-8.

<sup>8</sup> Zamore P. *Cell*. 2006;127:1083-1086.