AMVUTTRA® (vutrisiran)

Product Fact Sheet

- AMVUTTRA® (vutrisiran) is a U.S. Food and Drug Administration (FDA)-approved RNAi (RNA interference) therapeutic administered via subcutaneous injection once every three months for the treatment of the polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis in adults.
- hATTR amyloidosis is a rare, inherited disease characterized by symptoms that affect multiple body systems and is caused by the progressive deposition of toxic misfolded transthyretin (TTR) protein, which accumulates and leads to the manifestation of disease symptoms in multiple sites in the body, including the nerves, heart and digestive system.[1-4]
- AMVUTTRA works with the body's natural system to rapidly knock down TTR, addressing the underlying cause of hATTR amyloidosis.[3-5]
  - 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.[6]
- 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.[5]
  - 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.[5]
  - AMVUTTRA also improved other key measures of disease burden relative to external placebo.[5]
- AMVUTTRA demonstrated an acceptable safety and tolerability profile through 18 months of treatment.[5]
  - The most common adverse reactions were pain in extremity, arthralgia, dyspnea and vitamin A decreased.
- For more information about AMVUTTRA, please visit AMVUTTRA.com.

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

amvuttra (vutrisiran) injection 25 mg/0.5 mL

AMVUTTRA® (vutrisiran) Clinical Profile at a Glance[5]

- 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.[i]
  - 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 patients treated with AMVUTTRA 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.[ii]
    - Patients treated with AMVUTTRA also maintained a better walking speed[iii], experienced improvement in nutritional health[iv] and were better able to perform common daily activities at 18 months compared with placebo-treated patients.[v]
  - AMVUTTRA rapidly knocked down serum TTR as early as 3 weeks, with a mean TTR knockdown of 88% over 18 months.
  - 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%).[7]
- 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).

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

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[i] Higher scores indicate more severe disease (total score ranges from 0 to 304).

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

[iii] Evaluated using the 10-meter walk test, a stopwatch-timed measure of a patient's walking speed over 10 meters.

[iv] Evaluated using modified body mass index, an assessment of height, weight, and the balance of fluids in the body.

[v] 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.

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About RNAi Therapeutics

- RNAi 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.[8] This discovery was recognized with the award of the 2006 Nobel Prize for Physiology or Medicine.[9]
- 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.[8]

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.

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.

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AMV-USA-00147-V3