Vutrisiran: Arthralgia

The following information is provided in response to your unsolicited inquiry. It is intended to provide you with a review of the available scientific literature and to assist you in forming your own conclusions in order to make healthcare decisions. This document is not for further dissemination or publication without authorization.

The full Prescribing Information for AMVUTTRA® (vutrisiran) is provided here. Alnylam Pharmaceuticals does not recommend the use of its products in any manner that is inconsistent with the approved Prescribing Information. This resource may contain information that is not in the approved Prescribing Information.

If you are seeking additional scientific information related to Alnylam medicines, you may visit the Alnylam US Medical Affairs website at RNAiScience.com.

SUMMARY

- In the HELIOS-A study, arthralgia was reported as an AE in 13 patients (10.7%) in the vutrisiran group and 0 patients in the APOLLO-placebo group. The events were mostly mild or moderate in severity. None of the arthralgia events were serious, led to discontinuation or interruption of treatment, and did not increase over time.[1,2]
- In the HELIOS-B study, arthralgia was reported as an AE in 33 patients (10.1%) in the vutrisiran group and 39 patients (11.9%) in the placebo group.[3]
- A cumulative post-marketing review of Alnylam's global safety database did not identify any safety concerns involving arthralgia with the use of vutrisiran.[4]
- No additional information is available regarding arthralgia AEs and their management. The management of arthralgia is up to the clinical discretion of the healthcare provider.

INDEX

CLINICAL DATA

HELIOS-A

HELIOS-A was a phase 3, global, randomized, open-label study designed to evaluate the efficacy and safety of vutrisiran in patients with hATTR-PN. Patients were randomized (3:1) to receive either vutrisiran 25 mg every 3 months by subcutaneous injection (n=122) or patisiran 0.3 mg/kg every 3 weeks by IV infusion (as a reference group, n=42) for 18 months. This study used the placebo arm of the APOLLO study as an external control arm (n=77) for the primary endpoint and most other efficacy endpoints. The primary endpoint was the change from baseline in mNIS+7 at 9 months.[1]

During the 18-month treatment period, arthralgia was reported as an AE in 13 patients (10.7%) in the vutrisiran group, 4 patients (9.5%) in the patisiran group, and no patients in the APOLLO-placebo group. The AEs of arthralgia were mostly mild or moderate in severity, with 1 patient experiencing a severe AE. None of the AEs of arthralgia were serious, led to discontinuation or interruption of treatment, or study withdrawal. The AEs of arthralgia did not increase over time.[1,2]

HELIOS-B

HELIOS-B was a phase 3, global, randomized, double-blind, placebo-controlled, multicenter study designed to evaluate the efficacy and safety of vutrisiran in patients with ATTR-CM, including both hATTR and wtATTR. Patients were randomized (1:1) to receive either vutrisiran 25 mg (n=326) or placebo (n=329) every 3 months by subcutaneous injection for up to 36 months. The primary endpoint was the composite endpoint of all-cause mortality and recurrent CV events (CV hospitalizations and urgent heart failure visits) at the end of the double-blind period in the overall population and in the monotherapy population (patients not receiving tafamidis at baseline).[5]

During the double-blind period, arthralgia was reported as an AE in 33 patients (10.1%) in the vutrisiran group and 39 patients (11.9%) in the placebo group. Overall, the incidence of AEs among patients in the vutrisiran group was similar to or lower than that among patients in the placebo group, consistent with findings from the HELIOS-A study. There were no new safety concerns identified in the HELIOS-B study.[5]

GLOBAL SAFETY DATABASE

A cumulative post-marketing review of Alnylam Pharmaceuticals' global safety database did not identify any safety concerns involving arthralgia with the use of vutrisiran.[4]

AMVUTTRA PRESCRIBING INFORMATION – RELEVANT CONTENT

For relevant labeling information, please refer to the following section of the AMVUTTRA Prescribing Information[6]:

- ADVERSE REACTIONS Section 6.1 Clinical Trials Experience

ABBREVIATIONS

AE = adverse event; ATTR-CM = transthyretin amyloidosis with cardiomyopathy; CV = cardiovascular; hATTR = hereditary transthyretin amyloidosis; hATTR-PN = hereditary transthyretin amyloidosis with polyneuropathy; IV = intravenous; mNIS+7 = modified Neuropathy Impairment Score +7; wtATTR = wild-type transthyretin amyloidosis.

Updated 13 June 2025

REFERENCES

1. Adams D, Tournev IL, Taylor MS, et al. Efficacy and safety of vutrisiran for patients with hereditary transthyretin-mediated amyloidosis with polyneuropathy: a randomized clinical trial. *Amyloid*. 2023;30(1):18-26. doi:10.1080/13506129.2022.2091985
2. European Medicines Agency. Amvuttra : EPAR – Risk management plan. Published October 30, 2018. Updated June 12, 2025. Accessed June 13, 2025. https://www.ema.europa.eu/en/documents/rmp-summary/onpattro-epar-risk-management-plan-summary_en.pdf.
3. European Medicines Agency. Amvuttra-H-C-005852-II-0015 : EPAR - Assessment report – Variation. Published June 12, 2025. Accessed June 13, 2025. https://www.ema.europa.eu/en/documents/variation-report/amvuttra-h-c-005852-ii-0015-epar-assessment-report-variation_en.pdf.
4. Alnylam Pharmaceuticals. Data on file. MED-ALL-VUTRI-2500021.
5. Fontana M, Berk JL, Gillmore JD, et al. Vutrisiran in patients with transthyretin amyloidosis with cardiomyopathy. *N Engl J Med*. 2025;392(1):33-44. doi:10.1056/NEJMoa2409134
6. AMVUTTRA (vutrisiran) Prescribing Information. Cambridge, MA: Alnylam Pharmaceuticals, Inc.