Vutrisiran: Pain in Extremity

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SUMMARY

- In the HELIOS-A study, pain in extremity was reported in 18 (14.8%) patients in the vutrisiran arm over the 18-month treatment period; the events were mild or moderate in severity.[1,2]
- A cumulative post-marketing review of Alnylam's global safety database did not identify any new safety concerns involving pain in extremity with the use of vutrisiran.[3]
- No additional information is available regarding pain in extremity events and their management.

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CLINICAL DATA

HELIOS-A Study

HELIOS-A was a phase 3, global, randomized, open-label study designed to evaluate the efficacy and safety of vutrisiran in patients with the polyneuropathy of hATTR. 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 (NCT01960348) 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]

Pain in Extremity

Pain in extremity events during the HELIOS-A study were reported using the following preferred terms: "Pain in Extremity" and "Limb Discomfort". At 18 months of the HELIOS-A study, pain in extremity was reported in 18 (14.8%) of vutrisiran-treated patients compared with 8 (10.4%) of patients in the APOLLO placebo arm (**Table 1**). The AEs were mild or moderate in severity, and none of them led to treatment discontinuation. Pain in extremity AEs did not increase over time.[2]

Table 1. Pain in Extremity Events During the 18-Month Treatment Period of HELIOS-A.[1,a]

At least one event, n (%)	Placebo, APOLLO (n=77)	Vutrisiran, HELIOS-A (n=122)	Patisiran, HELIOS-A (n=42)
Pain in extremity	8 (10.4)	18 (14.8)	3 (7.1)

[a]Reported in the safety population during the 18-month treatment period.

GLOBAL SAFETY DATABASE

A cumulative post-marketing review of Alnylam Pharmaceuticals' global safety database did not identify any new safety concerns involving pain in extremity with the use of vutrisiran.[3]

AMVUTTRA PRESCRIBING INFORMATION – RELEVANT CONTENT

For relevant labeling information, please refer to the following section(s) of the AMVUTTRA Prescribing Information[4]:

- ADVERSE REACTION Section 6.1 Clinical Trials Experience

ABBREVIATIONS

AE = adverse event; hATTR = hereditary transthyretin amyloidosis; IV = intravenous; mNIS+7 = modified Neuropathy Impairment Score +7.

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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. Alnylam Pharmaceuticals. Data on file. MED-ALL-TTRSC02-2400021.
3. Alnylam Pharmaceuticals. Data on file. MED-ALL-TTRSC02-2400004.
4. AMVUTTRA (vutrisiran) Prescribing Information. Cambridge, MA: Alnylam Pharmaceuticals, Inc.