Vutrisiran: Dyspnea

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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.

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SUMMARY

- In the HELIOS-A study, dyspnea was reported in 8 (6.6%) patients in the vutrisiran arm over the 18-month treatment period; the events were mild or moderate in severity.[1]
- A cumulative post-marketing review of Alnylam's global safety database did not identify any new safety concerns involving dyspnea with the use of vutrisiran.[2]
- No additional information is available regarding dyspnea 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.[3]

Dyspnea

Dyspnea events during the HELIOS-A study were reported using the following preferred terms: Dyspnea, Dyspnea exertional, and Dyspnea paroxysmal nocturnal. At 18 months of the HELIOS-A study, dyspnea AEs were reported in 8 (6.6%) of patients treated with vutrisiran compared with 0 patients in the APOLLO placebo group. The AEs were mild to moderate in severity and did not lead to treatment interruption, treatment discontinuation, or withdrawal from a clinical study. The number of dyspnea AEs did not increase over time.[1] None of the dyspnea events were determined by the investigator to be related to treatment.[4]

GLOBAL SAFETY DATABASE

A cumulative post-marketing review of Alnylam Pharmaceuticals' global safety database did not identify any new safety concerns involving dyspnea with the use of vutrisiran.[2]

AMVUTTRA PRESCRIBING INFORMATION – RELEVANT CONTENT

For relevant labeling information, please refer to the following section(s) of the AMVUTTRA Prescribing Information[5]:

- ADVERSE REACTIONS Section 6.1 Clinical Trial Experience

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ABBREVIATIONS

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

REFERENCES

1. Alnylam Pharmaceuticals. Data on file. MED-ALL-TTRSC02-2400021.
2. Alnylam Pharmaceuticals. Data on file. MED-ALL-TTRSC02-2400004.
3. 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
4. Alnylam Pharmaceuticals. Data on file. MED-ALL-TTRSC02-2200045.
5. AMVUTTRA (vutrisiran) Prescribing Information. Cambridge, MA: Alnylam Pharmaceuticals, Inc.