

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Amyloidosis – Amvuttra Management Medical Policy

- Amvuttra™ (vutrisiran subcutaneous injection – Alnyam)

REVIEW DATE: 06/26/2024; selected revision 08/07/2024

OVERVIEW

Amvuttra, a transthyretin (TTR)-directed small interfering RNA, is indicated for the treatment of **polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR)** in adults.¹ Amvuttra has not been studied in patients with prior liver transplantation.⁵

Disease Overview

hATTR is a progressive disease caused by variants in the TTR gene leading to multisystem organ dysfunction.² Common neurologic manifestations include sensorimotor polyneuropathy, autonomic neuropathy, small-fiber polyneuropathy, and carpal tunnel syndrome.

Guidelines

There are no guidelines that include recommendations for Amvuttra. A scientific statement from the American Heart Association (AHA) on the treatment of the cardiomyopathy of hATTR amyloidosis (July 2020) includes recommendations related to polyneuropathy.³ Canadian guidelines for the treatment of patients with polyneuropathy (February 2021) include treatment recommendations for hATTR polyneuropathy as well.^{2,4} In general, Onpattro® (patisiran intravenous infusion) and Tegsedi® (inotersen subcutaneous injection) are recommended for patients with hATTR polyneuropathy.

For patients with hATTR amyloidosis with polyneuropathy, the AHA recommends treatment with Onpattro or Tegsedi.³ For patients with hATTR with polyneuropathy and cardiomyopathy, Onpattro, Tegsedi, or Vyndamax® (tafamidis meglumine capsules)/Vyndaqel™ (tafamidis capsules) are recommended. Use of combination therapy is discussed; however, it is noted that there is little data to support combination therapy.

The Canadian guidelines recommend Onpattro and Tegsedi as first-line treatment to stop the progression of neuropathy and improve polyneuropathy in early and late stage hATTR amyloidosis with polyneuropathy.²

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Amvuttra. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Amvuttra as well as the monitoring required for adverse events and long-term efficacy, approval requires Amvuttra to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

06/26/2024

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Coverage of Amvuttra is recommended in those who meet the following criteria:

FDA-Approved Indication

1. Polyneuropathy of Hereditary Transthyretin-Mediated Amyloidosis (hATTR). Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):

- A) Patient is ≥ 18 years of age; AND
- B) Patient has a transthyretin pathogenic variant as confirmed by genetic testing; AND
- C) Patient has symptomatic polyneuropathy; AND
Note: Examples of symptomatic polyneuropathy include reduced motor strength/coordination, and impaired sensation (e.g., pain, temperature, vibration, touch). Examples of assessments for symptomatic disease include history and clinical exam, electromyography, or nerve conduction velocity testing.
- D) Patient does not have a history of liver transplantation; AND
- E) The medication is prescribed by or in consultation with a neurologist, geneticist, or a physician who specializes in the treatment of amyloidosis.

Dosing. Approve the following dosing regimen (A and B):

- A) The dose is 25 mg by subcutaneous injection; AND
- B) The dose is administered not more frequently than once every 3 months.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Amvuttra is not recommended in the following situations:

1. Concomitant Use With Onpattro (patisiran intravenous infusion), Tegsedi (inotersen subcutaneous injection), Wainua (eplontersen subcutaneous injection), or a Tafamidis Product.

Note: Examples of tafamidis products are Vyndaqel and Vyndamax.

There are insufficient data supporting the safety and efficacy of concurrent use of these agents for hereditary transthyretin-mediated amyloidosis with polyneuropathy. The Vyndaqel/Vyndamax pivotal trial, which took place prior to when Onpattro and Tegsedi were under investigation for amyloidosis, did not include patients who were taking investigational drugs. The pivotal trials for Amvuttra, Onpattro, Tegsedi, and Wainua did not allow concurrent use of tetramer stabilizers (e.g., tafamidis, diflunisal). The pivotal trials for Amvuttra and Wainua did not allow concurrent use of Onpattro or Tegsedi (Amvuttra was not approved when Wainua was under investigation). A Phase II open-label extension study (n = 27) included 13 patients who were treated concomitantly with Onpattro and tafamidis.⁴ Following 24 months of treatment, there was no significant difference in the median serum transthyretin percent change from baseline with concomitant Onpattro and tafamidis (-80%) vs. Onpattro monotherapy (-88%). A scientific statement from the AHA notes that there is little data to support combination therapy for these products.³

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Amvuttra™ subcutaneous injection [prescribing information]. Cambridge, MA: Alnylam; February 2023.
2. Alcantara M, Mezi MM, Baker SK, et al. Canadian guidelines for hereditary transthyretin amyloidosis polyneuropathy management. *Can J Neuro Sci.* 2022;49:7-18.

3. Kittleston MM, Maurer MS, Ambardekar AV, et al; on behalf of the American Heart Association Heart Failure and Transplantation Committee of the Council on Clinical Cardiology. AHA scientific statement: cardiac amyloidosis: evolving diagnosis and management. *Circulation*. 2020;142:e7-e22.
4. Lin H, Merkel M, Hale C, Marantz JL. Experience of patisiran with transthyretin stabilizers in patients with hereditary transthyretin-mediated amyloidosis. *Neurodegener Dis Manag*. 2020;10(5):289-300.
5. Adams D, Tournev IL, Talor MS, et al. Efficacy and safety of vutrisitan for patients with hereditary transthyretin-mediated amyloidosis with polyneuropathy: a randomized clinical trial. *Amyloid*. 2023; 30(1):1-9.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	06/28/2023
Selected Revision	<p>Conditions Not Recommended for Approval</p> <p>Concomitant Use With Onpattro (patisiran intravenous injection), Tegsedi (inotersen subcutaneous injection), Wainua (eplontersen subcutaneous injection), or a Tafamidis Product. Wainua was added to this condition not recommended for approval.</p>	01/03/2024
Annual Revision	No criteria changes.	06/26/2024
Selected Revision	Polyneuropathy of Hereditary Transthyretin-Mediated Amyloidosis (hATTR): For diagnosis confirmed by genetic testing, rephrased the term “mutation” to “pathogenic variant”.	08/07/2024