PRIOR AUTHORIZATION POLICY

POLICY: Amyloidosis – Amvuttra Prior Authorization Policy
- Amvuttra™ (vutrisiran subcutaneous injection – Alnyam)

REVIEW DATE: 12/04/2024

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.[4]

Disease Overview

hATTR is a progressive disease caused by variants in the TTR gene leading to multisystem organ dysfunction.[2] Common neurologic manifestations include sensiomotor 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] 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 prescription benefit coverage of Amvuttra. 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

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 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.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Amvuttra is not recommended in the following situations:

1. **Concurrent use with other medications indicated for the treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis or transthyretin-mediated amyloidosis-cardiomyopathy (e.g., Attruby [acoramidis tablets], Onpattro [patisiran intravenous infusion], Tegsedi [inotersen subcutaneous injection], Wainua [eplontersen subcutaneous injection], or a tafamidis product).**
   The requested medication should not be administered in combination with other medications indicated for polyneuropathy of hereditary transthyretin-mediated amyloidosis or transthyretin-mediated amyloidosis-cardiomyopathy. Combination therapy is generally not recommended due to a lack of controlled clinical trial data supporting additive efficacy.

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 Nero Sci.* 2022;49:7-18.
3. Kittleson 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. 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.