CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Amyloidosis – Amvuttra Management Medical Policy
- Amvuttra™ (vutrisiran subcutaneous injection – Alnyam)

REVIEW DATE: 03/26/2025

OVERVIEW

Amvuttra, a transthyretin (TTR)-directed small interfering RNA, is indicated for the following uses:[1]
- **Polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR),** in adults.
- **Cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM),** in adults to reduce cardiovascular mortality, cardiovascular hospitalization, and urgent heart failure visits.

Disease Overview

ATTR is a progressive disease caused by variants in the TTR gene leading to multisystem organ dysfunction.[5] Although patients with ATTR may present with a variety of symptoms; neuropathy or cardiomyopathy are often the most prominent symptoms. Patients may also present with a mixed phenotype and exhibit signs of both neuropathy and cardiomyopathy.

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 American College of Cardiology expert consensus decision pathway on comprehensive multidisciplinary care for patients with cardiac amyloidosis (2023) recognizes tafamidis as a treatment option for ATTR-CM.[6] Early diagnosis is crucial since tafamidis slows the progression of the disease. It is noted that the benefit of tafamidis has not been observed in patients with New York Heart Association Class IV symptoms.

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 indications. 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

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

FDA-Approved Indications

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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.

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2. **Cardiomyopathy of Wild-Type or Hereditary Transthyretin-Mediated Amyloidosis (ATTR-CM).** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
   Note: Variant Transthyretin Amyloidosis is also known as Hereditary Transthyretin Amyloidosis.
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** The diagnosis was confirmed by ONE of the following (i, ii, or iii):
     - **i.** A technetium pyrophosphate scan (i.e., nuclear scintigraphy); OR
     - **ii.** A tissue biopsy with confirmatory transthyretin (TTR) amyloid typing by mass spectrometry, immunoelectron microscopy, or immunohistochemistry; OR
     - **iii.** Patient had genetic testing which, according to the prescriber, identified a transthyretin (TTR) pathogenic variant; AND
       Note: Examples of TTR variants include Val122Ile variant and Thr60Ala variant. If the patient has wild-type amyloidosis, this is **not** a TTR pathogenic variant.
   - **C)** Diagnostic cardiac imaging has demonstrated cardiac involvement; AND
     Note: Examples of cardiac imaging include echocardiogram and cardiac magnetic imaging. Examples of cardiac involvement on imaging include increased thickness of the ventricular wall or interventricular septum.
   - **D)** Patient has heart failure, but does **not** have New York Heart Association class IV disease; AND
   - **E)** The medication is prescribed by or in consultation with a cardiologist 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. **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.
5. US Department of Health and Human Services, National Institutes of Health. Transthyretin amyloidosis. Available at: https://ghr.nlm.nih.gov/condition/transthyretin-amyloidosis#diagnosis. Accessed on March 21, 2025.
6. Kittleson M, Ruberg FL, Ambardekar AV, et al. A report of the American College of Cardiology Solution Set Oversight Committee. 2023 ACC expert consensus decision pathway on comprehensive multidisciplinary care for the patient with cardiac amyloidosis. *J Am Coll Cardiol*. 2023;81(11):1076-1126.

HISTORY

Type of Revision	Summary of Changes	Review Date
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
Early Annual Revision	**Conditions Not Recommended for Approval:** 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) was changed to as listed (previously, concomitant use with Onpattro [patisiran intravenous injection], Tegsedi [inotersen subcutaneous injection], Wainua [eplontersen subcutaneous injection, or a Tafamidis product was listed.).	12/04/2024
Early Annual Revision	**Cardiomyopathy of Wild-Type or Hereditary Transthyretin-Mediated Amyloidosis (ATTR-CM):** This condition and criteria for approval were added to the policy.	03/26/2025