



Drug Coverage Policy

Effective Date 10/1/2024

Coverage Policy NumberIP0478

Policy Title.....Amyloidosis - Amvuttra

Amyloidosis – Amvuttra

- Amvuttra™ (vutrisiran subcutaneous injection – Alnyam)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna Healthcare Coverage Policy

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 mutations 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 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

Medical Necessity Criteria

Amvuttra is considered medically necessary when the following are met:

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.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

- 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

Coding / Billing Information

- 1) This list of codes may not be all-inclusive.
- 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J0225	Injection, vutrisiran, 1 mg

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. 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. 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 vutrisiran for patients with hereditary transthyretin-mediated amyloidosis with polyneuropathy: a randomized clinical trial. *Amyloid.* 2023; 30(1):1-9.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Review	<p>Polyneuropathy of Hereditary Transthyretin-Mediated Amyloidosis (hATTR).</p> <p>Removed 'Documentation that other causes of neuropathy have been excluded (for example, diabetes)'</p> <p>Updated 'Documented diagnosis of hereditary transthyretin-mediated (hATTR) amyloidosis confirmed by a transthyretin (<i>TTR</i>) genetic variant</p>	10/1/2024

	<p>(pathogenic or likely pathogenic variant)' to 'Patient has a transthyretin pathogenic variant as confirmed by genetic testing'</p> <p>Updated 'Documentation of symptomatic polyneuropathy confirmed by history and clinical exam, electromyography, or nerve conduction velocity' to 'Patient has symptomatic polyneuropathy; <u>Note</u>: 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.'</p> <p>Added to dosing 'The dose is administered not more frequently than once every 3 months.'</p> <p>Conditions Not Covered. Removed (1) Treatment of Cardiomyopathy hATTR in the Absence of Polyneuropathy Symptoms, (2) Treatment of Polyneuropathy Not Related to hATTR Amyloidosis.</p> <p>Updated title from "Vutrisiran' to 'Amyloidosis – Amvuttra'</p>	
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The policy effective date is in force until updated or retired.

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