Drug Coverage Policy

Effective Date.....10/01/2026
Coverage Policy Number.....IP0628
Policy Title.....Wainua

Amyloidosis – Wainua

- Wainua™ (eplontersen subcutaneous injection - AstraZeneca)

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 where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. 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.

OVERVIEW
Wainua, a transthyretin (TTR)-directed antisense oligonucleotide, is indicated for the treatment of the **polyneuropathy of hereditary TRR-mediated amyloidosis (hATTR)** in adults.[1] Wainua has not been studied in patients with prior liver transplantation. hATTR is a progressive disease caused by mutations 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 Wainua. 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) and recommendations from the European Society of Cardiology (ESC) [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]

The ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure note that TTR stabilization and reduction are the recommended basis of treatment for cardiomyopathy of hATTR.[4] Onpattro and Tegsedi may be considered for patients with hATTR polyneuropathy and cardiomyopathy.

Coverage Policy

POLICY STATEMENT
Prior Authorization is required for benefit coverage of Wainua. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Wainua as well as the monitoring required for adverse events and long-term efficacy, approval requires Wainua to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Documentation: Documentation is required where noted in the criteria as **[documentation required]**. Documentation may include, but not limited to, chart notes, laboratory tests, medical test results, genetic test results, claims records, and/or other information. All documentation must include patient-specific identifying information.

Wainua is considered medically necessary when the following is 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, E, and F):
   - **A)** Patient is ≥18 years of age; AND
   - **B)** Patient has a transthyretin pathogenic variant as confirmed by genetic testing **[documentation required]**; AND
   - **C)** Patient has symptomatic polyneuropathy **[documentation required]**; 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.

F) Preferred product criteria is met for the product as listed in the below table(s)

Dosing. Approve 45 mg subcutaneously once monthly.

Employer Plans:

Product	Criteria
Wainua Autoinjector (eplontersen subcutaneous injection)	**For Value, Advantage, Total Savings** Patient meets ONE of the following (1 or 2): 1. Patient has tried and, according to the prescriber, has experienced inadequate efficacy OR a significant intolerance with Amvuttra 2. Patient has already been started on therapy with Wainua
Wainua Prefilled Syringe (eplontersen subcutaneous injection)	Patient meets ONE of the following (1 or 2): 1. Patient has tried and, according to the prescriber, has experienced inadequate efficacy OR a significant intolerance with Amvuttra 2. Patient has already been started on therapy with Wainua

Individual and Family Plans:

Product	Criteria
Wainua Autoinjector (eplontersen subcutaneous injection)	Patient meets ONE of the following (1 or 2): 1. Patient has tried and, according to the prescriber, has experienced inadequate efficacy OR a significant intolerance with Amvuttra 2. Patient has already been started on therapy with Wainua
Wainua Prefilled Syringe (eplontersen subcutaneous injection)	Patient meets ONE of the following (1 or 2): 1. Patient has tried and, according to the prescriber, has experienced inadequate efficacy OR a significant intolerance with Amvuttra 2. Patient has already been started on therapy with Wainua

Conditions Not Covered

Wainua for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Concurrent use with other medications indicated for the treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis or transthyretin-mediated amyloidosis-cardiomyopathy (e.g., Amvuttra [vutrisiran subcutaneous injection],**

Attruby [acoramidis tablets], Onpattro [patisiran intravenous infusion], Tegsedi [inotersen 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.

Coding Information

Note: 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
C9311	Injection, eplontersen, 1 mg (code may be used for medicare when drug administered under the direct supervision of a physician, not for use when drug is self administered)
C9399	Unclassified drugs or biologicals (Code effective until 09/30/2026)
J3490	Unclassified drugs (Code effective until 09/30/2026)

References

1. Wainua™ subcutaneous injection [prescribing information]. Wilmington, DE: AstraZeneca; April 2025.
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. McDonagh TA, Metra M, Adamo M, et al. 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J.* 2021;42:3599-3726.
5. 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.
6. Coelho T, Ando Y, Benson MD, et al. Design and rationale of the global Phase 3 NEURO-TTransform Study of antisense oligonucleotide AKCEA-TTR-L_{rx} (ION-682884-CS3) in hereditary transthyretin-mediated amyloid polyneuropathy. *Neurol Ther.* 2021;10:375-389.

Revision Details

Summary of Changes	Review Date	Effective Date
New policy	05/02/2024	07/01/2024
Added "<u>Documentation</u>: Documentation is required where noted in the criteria. Documentation may include, but not limited to, chart notes,	01/30/2025	03/01/2025

laboratory tests, medical test results, genetic test results, claims records, and/or other information." **Polyneuropathy of Hereditary Transthyretin–Mediated Amyloidosis (hATTR)** **Updated** criteria **from** "Patient has a transthyretin pathogenic variant as confirmed by genetic testing" **to** "Documentation provided that the patient has a transthyretin pathogenic variant as confirmed by genetic testing." **Updated** criteria **from** "Patient has symptomatic polyneuropathy" **to** "Documentation provided that the patient has symptomatic polyneuropathy." **Conditions Not Covered** Concurrent use with other medications indicated for the treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis or transthyretin-mediated amyloidosis-cardiomyopathy (e.g., Amvuttra (vutrisiran subcutaneous injection), Attruby (acoramidis tablets), Onpattro (patisiran intravenous infusion), Tegsedi (inotersen subcutaneous injection), or a Tafamidis Product) was changed to as listed (previously Concomitant Use With Amvuttra (vutrisiran subcutaneous injection), Onpattro (patisiran intravenous infusion), Tegsedi (inotersen subcutaneous injection), or a Tafamidis Product). **Updated HCPCS Coding:** **Added** C9399		
Preferred Product Table. **Updated from "**Patient has tried Amvuttra; Patient has already been started on Wainua" **to** "Patient has tried and, according to the prescriber, has experienced inadequate efficacy OR a significant intolerance with Amvuttra; Patient has already been started on therapy with Wainua"	06/26/2025	09/01/2025
No criteria changes.	01/15/2026	03/01/2026
Preferred Product Table. **Employer Plans** **Added** "For Value, Advantage, Total Savings"	05/14/2026	07/01/2026
Preferred Product Table. **Employer Plans** **Clarified** the current requirements for Value, Advantage, Total Savings apply to the autoinjector. **Added** new preferred product requirements for Wainua prefilled syringes. Coding Information **Added HCPCS** C9311 **Updated** the description for C9399, J3490 to include the note "Code effective until 09/30/2026	08/27/2026	10/01/2026

The policy effective date is in force until updated or retired.

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