Drug Coverage Policy

Effective Date.....07/01/2024
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 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

Wainua, a transthyretin (TTR)-directed antisense oligonucleotide, is indicated for the treatment of the **polyneuropathy of hereditary transthyretin-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.

Medical Necessity Criteria

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

Employer Plans:

Product	Criteria
Wainua (eplontersen subcutaneous injection)	ONE of the following (1 or 2): 1. Patient has tried Amvuttra 2. Patient has already been started on Wainua

Individual and Family Plans:

Product	Criteria
Wainua (eplontersen	ONE of the following (1 or 2): 1. Patient has tried Amvuttra

Product	Criteria
subcutaneous injection)	2. Patient has already been started on Wainua

Dosing. Approve 45 mg subcutaneously once monthly.

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 Amvuttra (vutrisiran subcutaneous injection), Onpattro (patisiran intravenous infusion), Tegsedi (inotersen 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 Eplontersen was under investigation). A Phase II open-label extension study (n = 27) included 13 patients who were treated concomitantly with Onpattro and tafamidis.[5] 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 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
J3490	Unclassified drugs

References

1. Wainua™ subcutaneous injection [prescribing information]. Wilmington, DE: AstraZeneca; December 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. 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

Type of Revision	Summary of Changes	Date
New	New policy	07/01/2024

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