Clinical Policy: Eplontersen (Wainua)

Reference Number: PA.CP.PHAR.633
Effective Date: 05/2024
Last Review Date: 04/2025

Description
Eplontersen (Wainua™) is a transthyretin (TTR)-directed antisense oligonucleotide.

FDA Approved Indication(s)
Wainua is indicated for the treatment of polyneuropathy of hereditary TTR-mediated amyloidosis in adults.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Wainua is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Hereditary Transthyretin-Mediated Amyloidosis (must meet all)**:**

1. Diagnosis of hereditary TTR-mediated amyloidosis with polyneuropathy;
2. Documentation confirms presence of a TTR mutation;
3. Biopsy is positive for amyloid deposits or medical justification is provided as to why treatment should be initiated despite a negative biopsy or no biopsy;
4. Prescribed by or in consultation with a neurologist;
5. Age ≥ 18 years;
6. Member has not had a prior liver transplant;
7. Wainua is not prescribed concurrently with Onpattro, Tegsedi, or Amvuttra;
8. Dose does not exceed 45 mg once monthly.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Hereditary Transthyretin-Mediated Amyloidosis (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in any of the following parameters: measures of polyneuropathy (e.g., motor strength, sensation, and reflexes), quality of life, motor function, walking ability, and nutritional status (e.g., as evaluated by modified mass index);

3. Member has not had a prior liver transplant;
4. Wainua is not prescribed concurrently with Onpattro, Tegsedi, or Amvuttra;
5. If request is for a dose increase, new dose does not exceed 45 mg once monthly.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
TTR: transthyretin

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: General Information

- To confirm amyloidosis, the demonstration of amyloid deposits via tissue biopsy is essential. Deposition of amyloid in the tissue can be demonstrated by Congo red staining of biopsy specimens. With Congo red staining, amyloid deposits show a characteristic green birefringence under polarized light; however, negative biopsy results should not be interpreted as excluding the disease.
- DNA sequencing is usually required for genetic confirmation. Current techniques for performing sequence analysis of TTR, the only gene known to be associated with TTR amyloidosis, detect > 99% of disease-causing mutations.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Hereditary TTR-mediated amyloidosis with polyneuropathy	45 mg SC once monthly	45 mg/month

VI. Product Availability

Single-dose autoinjector: 45 mg/0.8 mL

VII. References

1. Wainua Prescriber Information. Wilmington, DE: AstraZeneca Pharmaceuticals; September 2024. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/217388s002lbl.pdf. Accessed January 9, 2024.
2. ClinicalTrials.gov. NEURO-TTRansform: A study to evaluate the efficacy and safety of eplontersen (Formerly Known as ION-682884, IONIS-TTR-LRx and AKCEA-TTR-LRx) in participants with hereditary transthyretin-mediated amyloid polyneuropathy. Available at: https://clinicaltrials.gov/ct2/show/NCT04136184. Accessed January 9, 2024.
3. Ando Y, Coelho T, Berk JL, et al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. Orphanet J Rare Dis. 2013 Feb 20;8:31.
4. Magrinelli F, Fabrizi GM, Santoro L, et al. Pharmacological treatment for familial amyloid polyneuropathy. Cochrane Database Syst Rev. 2020 Apr 20;4(4):CD012395.
5. Luigetti M, Romano A, Di Paolantonio A, et al. Diagnosis and treatment of hereditary transthyretin amyloidosis (hATTR) polyneuropathy: current perspectives on improving patient care. Therapeutics and Clinical Risk Management. 2020;16:109–23.
6. Coelho T, Marques W Jr, Dasgupta NR, et al.; NEURO-TTRansform Investigators. Eplontersen for Hereditary Transthyretin Amyloidosis With Polyneuropathy. JAMA. 2023 Oct 17; 330(15): 1448-1458.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
C9399	Unclassified drugs or biologicals
J3490	Unclassified drugs

Reviews, Revisions, and Approvals	Date
Policy created	04/2024
2Q 2025 annual review: removed criteria “member has not received prior treatment with, Onpattro or Amvuttra”; references reviewed and updated.	04/2025