Medical Drug Clinical Criteria

Subject:	Wainua (eplontersen)		
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Overview

This document addresses the use of Wainua (eplontersen), a transthyretin-directed antisense oligonucleotide approved by the Food and Drug Administration (FDA) for the treatment of polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis in adults. hATTR amyloidosis was formerly known as familial amyloid polyneuropathy (FAP). Wainua is administered via subcutaneous injection once monthly.

Hereditary transthyretin (hATTR) amyloidosis is a multisystemic, progressive, life-threatening disease characterized by extracellular deposition of amyloid fibrils composed of misfolded transthyretin (TTR), a plasma transport protein produced predominantly by the liver. Amyloid fibrils accumulate in various organs and tissues including the heart, kidney, gastrointestinal tract, and peripheral nerves, resulting in clinical manifestations such as polyneuropathy and cardiomyopathy. Potential symptoms associated with hATTR amyloidosis include but are not limited to muscle weakness, difficulty ambulating, impaired balance, orthostatic hypotension, disturbances in GI mobility, heart failure, arrhythmias and sudden death due to severe conduction disorders.

Due to the constellation of symptoms and multisystemic nature of the disease, various assessments need to be utilized in an effort to quantify the overall disease burden for each individual with hATTR amyloidosis. Examples of clinical tests include the Neuropathy Impairment Score (NIS) and Polyneuropathy Disability (PND) Score. Clinical trials evaluated the use of Wainua in individuals with hATTR amyloidosis and mild to moderate polyneuropathy. An example of mild to moderate polyneuropathy status is an individual who is able to ambulate with or without the use of assistance.

The efficacy of Wainua was demonstrated in an open-label, single-group, phase 3 trial in 168 adults with stage 1 (ambulatory) or stage 2 (ambulatory with assistance) hereditary transthyretin amyloidosis with polyneuropathy. Study participants had a Neuropathy Impairment Score (NIS) of 10-130 (NIS scale ranges from 0-244) and a TTR mutation confirmed by genotyping. Key exclusion criteria were previous or anticipated liver transplant, New York Heart Association (NYHA) class III or IV and other causes of polyneuropathy unrelated to hATTR amyloidosis. Individuals treated with placebo in a Tegsedi trial with similar eligibility criteria served as a historical placebo group. The primary efficacy assessments included change in serum transthyretin concentration, change in modified Neuropathy Impairment Score +7 (mNIS+7) composite score and change in Norfolk Quality of Life Questionnaire–Diabetic Neuropathy (Norfolk QoL-DN) total score; all favored Wainua over placebo.

Treatment with Wainua leads to a decrease in serum vitamin A levels. Individuals should be advised to take vitamin A supplementation at the recommended daily allowance while receiving Wainua therapy.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Wainua (eplontersen)

Initial requests for Wainua (eplontersen) may be approved if the following criteria are met:

I. Individual has a diagnosis of hereditary transthyretin (hATTR) amyloidosis or familial amyloid polyneuropathy (FAP); **AND**
II. Documentation is provided that individual has a TTR mutation verified by genotyping (Coelho 2023); **AND**
III. Documentation is provided that individual has associated mild to moderate polyneuropathy (Coelho 2023).

Continuation requests for Wainua (eplontersen) may be approved if the following criterion is met:

I. Documentation is provided that there is clinically significant improvement or stabilization in clinical signs and symptoms of disease (including but not limited to improved ambulation, improvement in neurologic symptom burden, improvement in activities of daily living).

Requests for Wainua (eplontersen) may not be approved for the following:

I. Individual has a history of or planned liver transplant; **OR**
II. Individual has severe renal impairment or end-stage renal disease; **OR**
III. Individual has moderate or severe hepatic impairment; **OR**
IV. Individual has New York Heart Association (NYHA) class III or IV functional class (Coelho 2023); **OR**
V. Individual has sensorimotor or autonomic neuropathy not related to hATTR amyloidosis (monoclonal gammopathy, autoimmune disease, etc.) (Coelho 2023); **OR**
VI. Individual is using in combination with Amvuttra, Onpattro, Tegsedi, Vyndaqel or Vyndamax; **OR**
VII. May not be approved when the above criteria are not met and for all other indications.

Quantity Limits

Wainua (eplontersen) Quantity Limit

Drug	Limit
Wainua (eplontersen) 45 mg/0.8 mL autoinjector	1 autoinjector per 28 days

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS	
J3490	Unclassified drugs (when specified as Wainua (eplontersen)
C9399	Unclassified drugs or biologicals
ICD-10 Diagnosis	
	All diagnoses pend

Document History

New: 1/4/2024
Document History:

- 1/4/2024 – Select Review: New criteria and quantity limit for Wainua. Coding Reviewed: Added HCPCS J3490, C9399. All diagnoses pend.

References

1. Ando Y, Coelho T, Berk JL, et. al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. *Orphanet J Rare Dis*. 2013;8(31).
2. Coelho T, Marques W Jr, Dasgupta NR, et al. Eplontersen for Hereditary Transthyretin Amyloidosis with Polyneuropathy. *JAMA*. 2023;330(15):1448-1458.
3. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: July 2, 2024.
4. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
5. Gertz MA, Benson MD, Dyck PJ, et. al. Diagnosis, Prognosis, and Therapy of Transthyretin Amyloidosis. *J Am Coll Cardiol*. 2015;66(21):2451-2466.
6. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.