Pharmacy Policy Bulletin: J-0826 Transthyretin-Directed Antisense Oligonucleotides – Commercial and Healthcare Reform	
Number: J-0826	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Injectable = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0826-010	**Original Date:** 11/07/2018
Effective Date: 07/18/2025	**Review Date:** 06/25/2025

Drugs Product(s):	• Wainua (eplontersen)
FDA-Approved Indication(s):	• Treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR) in adults

Background:	• Wainua (eplontersen) is a transthyretin-directed antisense oligonucleotide (ASO) that causes degradation of mutant and wild-type transthyretin (TTR) mRNA through binding to the TTR mRNA, which results in a reduction of serum TTR protein and TTR protein deposits in tissues. • Hereditary amyloidosis is an inherited, progressively debilitating disease caused by mutations in the TTR gene, which results in the accumulation of amyloid deposits in multiple organs of the body, including the nerves, heart, and the gastrointestinal tract. It is a rare disease currently impacting less than 3,000 individuals in the U.S. and 50,000 individuals worldwide, with a median survival of 4.7 years from diagnosis. • Wainua is the second FDA-approved transthyretin-directed antisense oligonucleotide for the treatment of the polyneuropathy of hATTR amyloidosis in adults. Tegsedi was the first FDA-approved transthyretin-directed ASO for the same indication; however, it is no longer available. Prior to Tegsedi, previous treatment options were limited to symptomatic management or liver transplant. • Wainua is administered as a 45 mg dose given as a subcutaneous (SC) injection once monthly. It can be administered by a healthcare professional, a caregiver or can be self-administered. Other gene therapies that are FDA-approved for the treatment of the polyneuropathy of hATTR amyloidosis include two small interfering RNAs (siRNAs): Onpattro (patisiran) and Amvuttra (vutrisiran). There is no data to support the safety and efficacy of combination gene therapies for the treatment of polyneuropathy of hATTR. All gene therapies pertaining to this indication have warnings for reduction of Vitamin A levels with therapy and potential risks for immunogenicity. • Manifestations of hereditary amyloidosis may vary depending on the organ

	system(s) impacted. Familial TTR is a multi-symptom disease that may present with peripheral neuropathy (sensory and motor), autonomic neuropathy, gastrointestinal impairment, cardiomyopathy, nephropathy, or ocular deposition.
	• Performance Stages or Scores
	  ○ Familial amyloidotic polyneuropathy (FAP) stage include:
	  ▪ Stage 1: unimpaired ambulation
	  ▪ Stage 2: assistance with ambulation required
	  ▪ Stage 3: wheelchair bound or bedridden
	  ○ The Neuropathic Impairment Score (NIS) ranges from 0 to 244 points with a higher score indicating poorer function.
	  ○ Polyneuropathy disability (PND) score ranges from
	  ▪ I: preserved walking, sensory disturbances
	  ▪ II: impaired walking but can walk without stick or crutch
	  ▪ IIIa: walk with 1 stick or crutch
	  ▪ IIIb: walk with 2 sticks or crutches
	  ▪ IV: confined to wheelchair or bedridden
	  ○ In clinical trials pertaining to Wainua, functional ambulation performance stage 1 (patient is ambulatory) or stage 2 (patient is ambulatory with assistance) was required for patients to be included in the trial. Additionally, an NIS score ≥10 and ≤130 was required for patients to be included in the trial. Guidelines recommend patients should receive disease-modifying pharmacotherapy only within the confines of a clinical trial.
	  ○ After diagnosis, patients are followed up every ~6 months and assessed for new or progressed symptoms and functional scores for polyneuropathy disability. When polyneuropathy is present, it shows as sensorimotor polyneuropathy and autonomic dysfunction. As Wainua is used to treat polyneuropathy, it is appropriate to assess that the medication administered is providing patient improvement.
	• Prescribing Considerations:
	  ○ The ideal setting for evaluation of the individual with hereditary transthyretin amyloidosis is a multi-disciplinary Amyloid Program.
	  ○ Platelet clumping can cause uninterpretable platelet measurement; repeat test if this is suspected.
	  ○ Monitor for serious neurologic adverse reactions consistent with inflammatory and immune effects.

Approval Criteria

I. Initial Authorization

When a benefit, coverage of Wainua may be approved when all the following criteria are met **(A. through H.)**:

A. The member is 18 years of age or older.

B. Prescribed by or in consultation with a neurologist or physician who specializes in the treatment of amyloidosis.

C. The member has a diagnosis of polyneuropathy associated with hereditary transthyretin-mediated amyloidosis (hATTR).

D. There is documentation of a mutation in the TTR gene confirmed by genetic testing.

E. A complete neurologic examination has been performed, showing clinical signs and symptoms of the disease (e.g., peripheral/autonomic neuropathy, motor disability, carpal tunnel, etc.).

F. The prescriber attests that the member meets one (1) of the following baseline performance status **(1. or 2.)**:

1. Ambulatory (stage 1)

2. Ambulatory with assistance (stage 2)

G. The prescriber attests that the member meets one (1) of the following parameters **(1. or 2.)**:

1. NIS ≥ 10

2. PND score of I, II, IIIa, or IIIb

H. The member is not simultaneously utilizing transthyretin-lowering agents other than the requested drug (for example, Amvuttra, Attruby, Vyndaqel, Vyndamax, or Onpattro).

II. Reauthorization

When a benefit, reauthorization of Wainua may be approved when all the following criteria are met **(A., B., and C.)**:

A. Prescribed by or in consultation with a neurologist or physician who specializes in the treatment of amyloidosis.

B. The member is not simultaneously utilizing other gene targeted therapy for polyneuropathy of hATTR.

C. The prescriber attests that the member has experienced positive clinical response to therapy defined as improvement or stabilization of one (1) of the following **(1., 2., or 3.)**:

1. FAP status/stage

2. NIS score

3. PND score

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

References:

1. Wainua [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; April 2025.
2. Benson, M.D., Waddington-Cruz M., Berk, J.L. et al. Inotersen Treatment for Patients with Hereditary Transthyretin Amyloidosis. *The New England Journal of Medicine*. 2018; 379:22-31.
3. Ando Y, Coelho T, Berk JL, et al., Guideline of transthyretin-related hereditary amyloidosis for clinicians. *Orphanet J. Rare Dis.* 2013;8(1):1-18.
4. Adams D, Ando Y, Beirao JM, et al., Expert consensus recommendations to improve diagnosis of ATTR amyloidosis with polyneuropathy. *J Neurol*. 2021;268(6):2109-2122.