eplontersen (Wainua™)

EOCCO POLICY

Policy Type:PA/SP Pharmacy Coverage Policy: EOCCO303

Description

Eplontersen (Wainua) is a subcutaneously administered antisense oligonucleotide inhibitor.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit
eplontersen (Wainua)	Hereditary transthyretin amyloidosis (hATTR) with polyneuropathy	45 mg/0.8 mL auto-injector	0.8mL/28 days

Initial Evaluation

I. **Eplontersen (Wainua)** may be considered medically necessary when the following criteria are met:
   A. Medication is prescribed by, or in consultation with, a neurologist or cardiologist; **AND**
   B. Member is 18 years of age or older; **AND**
   C. Medication is not used in combination with any other TTR silencer therapy (i.e., inotersen (Tegsedi), patisiran (Onpattro), tafamidis meglumine (Vyndaqel)); **AND**
   D. A diagnosis of **hereditary transthyretin amyloidosis (hATTR) with polyneuropathy** confirmed by:
      1. Documentation of amyloid deposit via biopsy; **AND**
      2. Documentation of transthyretin variant (TTR mutation) by genotyping (e.g., V30M); **AND;**
      ~~3.~~ Confirmation of <u>one</u> of the following baseline measures:
         i. A baseline polyneuropathy disability (PND) score less than, or equal to, IIIb; **OR**
         ii. A baseline Coutinho stage score less than, or equal to, two; **AND**
   E. Presence of clinical signs and symptoms of the disease (e.g., peripheral sensorimotor polyneuropathy, autonomic neuropathy, motor disability, etc.); **AND**
   F. Member has <u>not</u> received or is not anticipating a liver transplant; **AND**
   G. Member does <u>not</u> have New York Heart Association (NYHA) functional class ≥ III heart failure

II. Eplontersen (Wainua) is considered <u>investigational</u> when used for all other conditions, including but <u>not limited to</u>:

A. Cardiac amyloidosis due to wild-type or mutant TTR.
B. Transthyretin amyloidosis of the wild-type origin (ATTRwt)
C. Pediatrics and adolescents under the age of 18 years old
D. When used in combination with other TTR silencer therapy (i.e., inotersen (Tegsedi), patisiran (Onpattro), tafamidis meglumine (Vyndaqel)).

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Documentation that the patient has experienced a positive clinical response to eplontersen (Wainua) (e.g., improved neurologic impairment, motor function, quality of life, slowing of disease progression, etc.); **AND**
IV. Continued confirmation of one of the following:
    A. Polyneuropathy disability (PND) score less than or equal to stage IIIb; **OR**
    B. Coutinho stage score less than or equal to two; **AND**
V. Eplontersen (Wainua) will not be used in combination with other with other therapies for hATTR (i.e., patisiran (Onpattro) or tafamidis meglumine (Vyndaqel); **AND**
VI. Member has not received or is not anticipating a liver transplant; **AND**
VII. Member does not have New York Heart Association (NYHA) functional class ≥ III heart failure

Supporting Evidence

I. Hereditary transthyretin amyloidosis (hATTR) with polyneuropathy is a rare, inherited disease that occurs due to mutations in the gene encoding transthyretin (TTR). Inherited mutations of the TRR gene are categorized into two main phenotypes: ATTRv with polyneuropathy (ATTRv-PN) and ATTRv with cardiomyopathy (ATTRv-CM). Eplontersen (Wainua) is currently approved for ATTRv-PN only.
II. Hereditary transthyretin amyloidosis is a systemic, progressively debilitating, and fatal disease caused by the misfolding, deposition, and accumulation of transthyretin (TTR) amyloid fibrils in multiple organs. Clinical course is variable and typically includes increased multiorgan involvement with progression of disease. Median survival is about ten years from disease onset. The goals of treatment include preventing disease progression, treating multiorgan involvement, reducing function loss, and preserving quality of life.
III. Eplontersen (Wainua) was studied in a Phase 3, multicenter, open-label, randomized, 6:1, historical placebo-controlled trial consisting of 144 subjects (NEURO-TTRansform study). Subjects included in the interim analysis had stage one or two ATTRv-PN (defined by either

Coutinho staging or polyneuropathy disability [PND] score). Participants were excluded if they had received previous treatment with TRR silencers or had previously undergone a liver transplant. The mean subject age was 53 years, the majority being male, with V30M genetic mutation, stage one ATTRv-PN, less severe mobility at baseline, of non-US geographical region, and of the mixed cardiomyopathy phenotype.

IV. There are currently no official evidence-based guidelines specifically for the diagnosis of ATTRv-PN in the U.S. The American College of Cardiology (ACC) 2023 guidelines recommend diagnosis of ATTRv with a cardiologist as the designated primary clinician. The American Heart Association (AHA) 2020 guidelines also recommend diagnosis and treatment under either a neurologist or cardiologist.

V. Safety and efficacy of eplontersen (Wainua) use in patients under the age of 18 has not been well-established. There is currently a lack of sufficient evidence or additional scientific literature to support the use of eplontersen (Wainua) in members under 18 years of age.

VI. Safety and efficacy of using eplontersen (Wainua) in combination with other TTR silencer therapies for hATTR (i.e., patisiran (Onpattro) or tafamidis meglumine (Vyndaqel) has not been studied. There is currently a lack of sufficient evidence or additional scientific literature to support the use of eplontersen (Wainua) in combination with other TTR silencer therapy.

VII. The American Heart Association (AHA) and American College of Cardiology (ACC) guideline recommendations for the diagnosis of amyloidosis are specific for the cardiomyopathy phenotype. The Journal of Neurology (2020) offers expert consensus recommendations specifically for the diagnosis of ATTRv-PN. Diagnosis of the hereditary form of ATTR requires deoxyribonucleic acid (DNA) sequencing and a biopsy. Deoxyribonucleic acid sequencing reveals the TTR gene mutation indicative of hereditary versus wild-type forms of ATTR. A biopsy is required to detect the presence of amyloid fibrils. Deoxyribonucleic acid sequencing and biopsy results are definitive for confirmation of hATTR. Eplontersen (Wainua) is not FDA-indicated for use in wild-type amyloidosis.

VIII. The Journal of Neurology recommends staging of ATTRv-PN with either the Coutinho staging score or the polyneuropathy disability (PND) staging score to assess for mobility, ambulation, and neuropathy severity. The NEURO-TTRansform study only included subjects that had earlier, less severe forms of ATTRv-PN (defined by either Coutinho staging 1 or 2, or polyneuropathy disability [PND] score ≤IIIb). Patients with more severe staging of ATTRv-PN were excluded. There is currently lack of sufficient evidence to support the safety and efficacy of eplontersen (Wainua) in patients with more severe forms of disease.

IX. Symptoms of ATTRv-PN commonly start with lower limb impairment, orthostatic hypotension, and gastrointestinal disturbances, but later lead to progressive muscle wasting, central nervous system dysfunction, renal impairment, and increasingly substantial functional impairment.

X. Studies suggest that orthotopic liver transplantation causes prompt replacement of variant transthyretin by the donor wild type in the plasma. The NEURO-TTRansform study excluded patients who had previously received a liver transplant or are anticipating liver transplant within one year of screening. There is currently insufficient evidence to evaluate the efficacy of eplontersen (Wainua) in treatment of patients who are refractory to or anticipating liver

transplant. Phase 3 trials studying the safety and efficacy of TTR silencer therapy in this disease space also exclude patients with prior or anticipated liver transplant.

XI. The NEURO-TTRansform study excluded patients who had a New York Hearth Association (NYHA) functional classification score of ≥ III heart failure. There is currently insufficient evidence to support the efficacy and safety of eplontersen (Wainua) in the treatment of patients who have more severe cardiovascular disease. According to ACC 2023 guidelines, "…patients with advanced [cardiac disease], treatment aimed at TTR stabilization is unlikely to be of significant benefit.".

Investigational or Not Medically Necessary Uses

I. Eplontersen (Wainua) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. Cardiac amyloidosis due to wild-type or mutant TTR
      i. Eplontersen (Wainua) in the cardiac amyloidosis setting (sans polyneuropathy involvement) is currently under investigation in a Phase 3, multicenter, double-blinded study (CARDIO-TTRansform trial). It is currently in the active study phase, estimated to be completed in June of 2025.
   B. Transthyretin amyloidosis of the wild-type origin (ATTRwt)
      i. Pivotal trials leading to FDA approval of eplontersen (Wainua) were specifically in the hereditary transthyretin-mediated amyloidosis setting. Wild-type TTR is not considered hereditary. There are currently no ongoing or active trials to study the use of eplontersen (Wainua) in the non-hereditary disease space. There is currently a lack of sufficient evidence or additional scientific literature to support the use of eplontersen (Wainua) for ATTRwt.
   C. Pediatrics and adolescents under the age of 18 years old
      i. There are currently no ongoing or active trials to study the use of eplontersen (Wainua) in pediatric patients less than 18 years of age. There is currently a lack of sufficient evidence or additional scientific literature to support the use of eplontersen (Wainua) in members less than 18 years of age.
   D. Use of eplontersen (Wainua) in combination with other TTR silencer therapy (i.e., inotersen (Tegsedi), patisiran (Onpattro), tafamidis meglumine (Vyndaqel)).
      i. There are currently no ongoing or active trials to study the use of eplontersen (Wainua) in combination with other TTR silencer therapy. There is currently a lack of additional scientific literature to support the use of eplontersen (Wainua) in combination with other TTR silencers.

References

1. Approved eplontersen (Wainua) Dossier. AstraZeneca. December, 2023.
2. WAINUA. Prescribing information. Astrazeneca Pharmaceuticals LP; 2023
3. Coelho, Teresa et al. "Eplontersen for Hereditary Transthyretin Amyloidosis With Polyneuropathy." JAMA vol. 330,15 (2023): 1448-1458.
4. Writing Committee et al. "2023 ACC Expert Consensus Decision Pathway on Comprehensive Multidisciplinary Care for the Patient With Cardiac Amyloidosis: A Report of the American College of Cardiology Solution Set Oversight Committee." Journal of the American College of Cardiology vol. 81,11 (2023): 1076-1126. doi:10.1016/j.jacc.2022.11.022
5. Kittleson, Michelle M et al. "Cardiac Amyloidosis: Evolving Diagnosis and Management: A Scientific Statement From the American Heart Association." Circulation vol. 142,1 (2020): e7-e22.
6. Adams, David et al. "Expert consensus recommendations to improve diagnosis of ATTR amyloidosis with polyneuropathy." Journal of neurology vol. 268,6 (2021): 2109-2122. doi:10.1007/s00415-019-09688-0
7. Luigetti, Marco et al. "Diagnosis and Treatment of Hereditary Transthyretin Amyloidosis (hATTR) Polyneuropathy: Current Perspectives on Improving Patient Care." Therapeutics and clinical risk management vol. 16 109-123. 21 Feb. 2020
8. Vélez-Santamaría, Valentina et al. "Hereditary Transthyretin Amyloidosis with Polyneuropathy: Monitoring and Management." International journal of general medicine vol. 15 8677-8684. 20 Dec. 2022, doi:10.2147/IJGM.S338430

Related Policies

Policies listed below may be related to the current policy. Related policies are identified based on similar indications, similar mechanisms of action, and/or if a drug in this policy is also referenced in the related policy.

Policy Name	Disease state
inotersen (TEGSEDI®)	Hereditary transthyretin-mediated amyloidosis with polyneuropathy
tafamidis meglumine (Vyndaqel®); tafamidis (Vyndamax™)	Cardiomyopathy of wide type (ATTRwt-CM); Hereditary transthyretin-mediated amyloidosis (hATTR-CM)

Policy Implementation/Update:

Action and Summary of Changes	Date
Policy created	05/2024