Mass General Brigham
Health Plan

Wainua (eplontersen)
Effective 07/01/2025

Plan	☐ MassHealth UPPL ☒Commercial/Exchange	**Program Type**	☒ Prior Authorization ☐ Quantity Limit ☐ Step Therapy
Benefit	☒ Pharmacy Benefit ☐ Medical Benefit		
Specialty Limitations	This medication has been designated specialty and must be filled at a contracted specialty pharmacy.		
Contact Information	**Medical and Specialty Medications** All Plans | Phone: 877-519-1908 | Fax: 855-540-3693		
	Non-Specialty Medications All Plans | Phone: 800-711-4555 | Fax: 844-403-1029		
Exceptions	N/A		

Overview
Wainua (eplontersen) is a transthyretin-directed antisense oligonucleotide indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

Coverage Guidelines
Authorization may be reviewed for members new to the plan within the last 90 days who are currently receiving treatment with the requested medication, excluding when the product is obtained as samples or via manufacturer's patient assistance programs.
OR
Authorization may be granted for members when ALL the following criteria are met:

1. Member has a diagnosis of polyneuropathy of hereditary transthyretin-mediated amyloidosis (hAATR-PN)
2. Diagnosis is confirmed by documentation of presence of a transthyretin (TTR) mutation (e.g., V30M)
3. Member is 18 years of age or older
4. Member is experiencing clinical signs and symptoms of polyneuropathy, defined as ONE of the following:
    a. Polyneuropathy disability (PND) score ≤ IIIb
    b. Stage 1 or 2 familial amyloidotic polyneuropathy (FAP) or Coutinho stage
    c. Neuropathy Impairment Scale score ≥ 10 and ≤ 130
5. Prescribed by or in consultation with a neurologist
6. Requested medication will not be used in combination with a TTR silencer (e.g., Amvuttra) or a TTR stabilizer (e.g., diflunisal, Attruby, Vyndamax, or Vyndaqel)

<u>Continuation of Therapy</u>
Requestions for reauthorization will be approved when the following criteria are met:

1. Documentation member has had a positive clinical response to therapy (e.g., improved quality of life, improved or stable motor function, decreased serum TTR level)

Limitations

1. Initial and reauthorization approvals will be authorized for 12 months.
2. The following quantity limitations apply:

Drug Name and Dosage Form	Quantity Limit
Wainua injection	1 injection per 28 days

References

1. Barroso FA, Judge DP, Ebede B, et al. Long-term safety and efficacy of tafamidis for the treatment of hereditary transthyretin amyloid polyneuropathy: results up to 6 years. *Amyloid*. 2017;24(3):194-204.
2. Benson MD, Dasgupta NR, Rissing SM, Smith J, Feigenbaum H. Safety and efficacy of a TTR specific antisense oligonucleotide in patients with transthyretin amyloid cardiomyopathy. *Amyloid*. 2017;24(4):217-223.
3. Benson MD, Waddington-Cruz M, Berk JL, et al. Inotersen treatment for patients with hereditary transthyretin amyloidosis. *N Engl J Med*. 2018;379:22-31.
4. Berk JL, Suhr OB, Obici L, et al for the Diflunisal Trial Consortium. Repurposing diflunisal for familial amyloid polyneuropathy: a randomized clinical trial. *JAMA*. 2013;310(24):2658-2667.
5. Brannagan TH, Wang AK, Coelho T, et al. Early data on long-term efficacy and safety of inotersen in patients with hereditary transthyretin amyloidosis: a 2-year update from the open-label extension of the NEURO-TTR trial. *Eur J Neurol.* 2020;27:1374-1381.
6. Buxbaum JN, Ruberg FL. Transthyretin V122I (pV142I)* cardiac amyloidosis: an age dependent autosomal dominant cardiomyopathy too common to be overlooked as a cause of significant heart disease in elderly African Americans. *Genet Med*. 2017;19(7):733-742.
7. Buxbaum JN. Oligonucleotide drugs for transthyretin amyloidosis. *N Engl J Med*. 2018;379-381.
8. Carroll A, Dyck PJ, de Carvalho M, et al. Novel approaches to diagnosis and management of hereditary transthyretin amyloidosis. *J Neurol Neurosurg Psychiatry*. 2022;93:668-678. doi: 10.1136/jnnp-2021-327909.
9. Coelho T, Adams D, Conceicao I, et al. A phase II, open-label, extension study of long-term patisiran treatment in patients with hereditary transthyretin-mediated (hATTR) amyloidosis. *Orphanet J Rare Dis*. 2020;15:179.
10. Coelho T, Conceicao I, Waddington-Cruz M, et al on behalf of the THAOS investigators. A natural history analysis of asymptomatic TTR gene carriers as they develop symptomatic transthyretin amyloidosis in the Transthyretin Amyloidosis Outcomes Survey (THAOS). *Amyloid*. 2022. doi: 10.1080/13506129.2022.2070470.
11. Coelho T, Maia LF, da Silva AM, et al. Long-term effects of tafamidis for the treatment of transthyretin familial amyloid polyneuropathy. *J Neurol.* 2013[a];260:2802-2814.
12. Coelho T, Maia LF, Martins da SA, et al. Tafamidis for transthyretin familial amyloid polyneuropathy: a randomized, controlled trial. *Neurology*. 2012;79:785-792.
13. Coelho T, Marques W Jr, Dasgupta NR, et al. Eplontersen for hereditary transthyretin amyloidosis with polyneuropathy. *JAMA*. 2023;330(15):1448-1458.
14. Coelho T, Maurer MS, Suhr OB. THAOS - The Transthyretin Amyloidosis Outcomes Survey: initial report on clinical manifestations in patients with hereditary and wild type transthyretin amyloidosis. *Curr Med Res Opin.* 2013[b];29(1):63-76.

15. Damy T, Garcia-Pavia P, Hanna M, et al. Efficacy and safety of tafamidis doses in the tafamidis in transthyretin cardiomyopathy clinical trial (ATTR-ACT) and long-term extension study. *Eur J Heart Failure*. 2021;23:277-285.
16. Dasgupta NR, Rissing SM, Smith et al. Inotersen therapy of transthyretin amyloid cardiomyopathy. *Amyloid*. 2020;27(1):52-58.
17. Dispenzieri A, Coelho T, Conceicao I, et al on behalf of the THAOS investigators. Clinical and genetic profile of patients enrolled in the Transthyretin Amyloidosis Outcomes Survey (THAOS): 14-year updated. *Orphanet J Rare Dis*. 2022;17:236.
18. Dorbala S, Ando Y, Bokhari et al. ASNC/AHA/ASE/EANM/HFSA/ISA/SCMR/SNMMI expert consensus recommendations for multimodality imaging in cardiac amyloidosis. Part 2 of 2 – diagnostic criteria and appropriate utilization. *Circ Cardiovasc Imaging*. 2021[b];14:e000030. doi: 10.1161/HCI.0000000000000030.
19. Dorbala S, Ando Y, Bokhari et al. ASNC/AHA/ASE/EANM/HFSA/ISA/SCMR/SNMMI expert consensus recommendations for multimodality imaging in cardiac amyloidosis. Part 1 of 2 – evidence base and standardized methods of imaging. *Circ Cardiovasc Imaging*. 2021[a];14:e000029. doi: 10.1161/HCI.0000000000000029.
20. Dyck PJB, González-Duarte A, Obici L, et al. Development of measures of polyneuropathy impairment in hATTR amyloidosis: from NIS to mNIS+7. *J Neurol Sci*. 2019;405:116424.
21. Elliot P, Drachman GM, Gottlieb SS, et al. Long-term survival with tafamidis in patients with transthyretin amyloid cardiomyopathy. *Circ Heart Failure*. 2022;15:e008193. doi: 10.1161/circheartfailure.120.008193.
22. Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2022;79:e263-e421.
23. Kittleson MK, Maurer MS, Ambardekar AV, at al. Cardiac amyloidosis: evolving diagnosis and management: a scientific statement from the American Heart Association. *Circ*. 2020;142:e7-e22. doi: 10.1161/CIR.0000000000000792.
24. Klaassen SHC, Tromp J, Nienhuis HLA, et al. Involvement at presentation in hereditary transthyretin-derived amyloidosis and the value of N-terminal pro-B-type natriuretic peptide. *Am J Cardiol*. 2018;121:107-112.
25. Magrinelli F, Fabrizi GM, Santoro L, et al. Pharmacological treatment for familial amyloid polyneuropathy. *Cochrane Database Syst Rev*. 2020;4:CD012395.
26. Maurer MS, Grogan DR, Judge DP, et al. Tafamidis in transthyretin amyloid cardiomyopathy. Effects on transthyretin stabilization and clinical outcomes. *Circ Heart Fail*. 2015;8:519-526.
27. Rossor AM, Reilly MM, Sleigh JN. Antisense oligonucleotides and other genetic therapies made simple. *Pract Neurol*. 2018;18:126-131.
28. Waddington-Cruz M, Ackermann EJ, Polydefkis M, et al. Hereditary transthyretin amyloidosis: baseline characteristics of patients in the NEURO-TTR trial. *Amyloid*. 2018;25(3):180-188.
29. Wainua (eplontersen) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals. September 2024.
30. Yarlas A, Lovely A, Brown D, et al. Responder analysis for neuropathic impairment and quality-of-life assessment in patients with hereditary transthyretin amyloidosis with polyneuropathy in the NEURO-TTR study. *J Neurol*. 2022;269:323-335.

Review History
09/11/2024 – Reviewed for September P&T. Effective 11/1/2024.
04/09/2025 – Reviewed at April P&T. Updated initial criteria to: provide an example of a TTR mutation; clarify that member must be experiencing clinical signs and symptoms of polyneuropathy; require that Wainua is prescribed by or in consultation with a neurologist; include Attruby as an example of a TTR stabilizer that should not be co-prescribed with Wainua. Updated reauthorization criteria to include examples of positive clinical response to therapy. Effective 07/01/2025.