PRIOR AUTHORIZATION POLICY

POLICY: Amyloidosis – Wainua Prior Authorization Policy
- Wainua™ (eplontersen subcutaneous injection – AstraZeneca)

REVIEW DATE: 12/04/2024

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Wainua, a transthyretin (TTR)-directed antisense oligonucleotide, is indicated for the treatment of the **polyneuropathy of hereditary TRR-mediated amyloidosis (hATTR)** in adults.[1] Wainua has not been studied in patients with prior liver transplantation. hATTR is a progressive disease caused by mutations in the TTR gene leading to multisystem organ dysfunction.[2] Common neurologic manifestations include sensiomotor polyneuropathy, autonomic neuropathy, small-fiber polyneuropathy, and carpal tunnel syndrome.

Guidelines

There are no guidelines that include recommendations for Wainua. A scientific statement from the American Heart Association (AHA) on the treatment of the cardiomyopathy of hATTR amyloidosis (July 2020) includes recommendations related to polyneuropathy.[3] Canadian guidelines for the treatment of patients with polyneuropathy (February 2021) and recommendations from the European Society of Cardiology (ESC) [2021] include treatment recommendations for hATTR polyneuropathy as well.[2,4] In general, Onpattro® (patisiran intravenous infusion) and Tegsedi® (inotersen subcutaneous injection) are recommended for patients with hATTR polyneuropathy.

For patients with hATTR amyloidosis with polyneuropathy, the AHA recommends treatment with Onpattro or Tegsedi.[3] For patients with hATTR with polyneuropathy and cardiomyopathy, Onpattro, Tegsedi, or Vyndamax® (tafamidis meglumine capsules)/Vyndaqel™ (tafamidis capsules) are recommended. Use of combination therapy is discussed; however, it is noted that there is little data to support combination therapy.

The Canadian guidelines recommend Onpattro and Tegsedi as first-line treatment to stop the progression of neuropathy and improve polyneuropathy in early and late stage hATTR amyloidosis with polyneuropathy.[2]

The ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure note that TTR stabilization and reduction are the recommended basis of treatment for cardiomyopathy of hATTR.[4] Onpattro and Tegsedi may be considered for patients with hATTR polyneuropathy and cardiomyopathy.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Wainua. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Wainua as well as the monitoring required for adverse events and long-term efficacy, approval requires Wainua to be prescribed by or in consultation with a physician who specializes in the condition being treated.

- **Wainua™ (eplontersen subcutaneous injection - AstraZeneca)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indication

1. **Polyneuropathy of Hereditary Transthyretin-Mediated Amyloidosis (hATTR).** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
   Note: Variant Transthyretin Amyloidosis is also known as Hereditary Transthyretin Amyloidosis.
   A) Patient is ≥18 years of age; AND
   B) Patient has a transthyretin (TTR) pathogenic variant as confirmed by genetic testing; AND
   C) Patient has symptomatic polyneuropathy; AND
   Note: Examples of symptomatic polyneuropathy include reduced motor strength/coordination, and impaired sensation (e.g., pain, temperature, vibration, touch). Examples of assessments for symptomatic disease include history and clinical exam, electromyography, or nerve conduction velocity testing.
   D) Patient does **not** have a history of liver transplantation; AND

E) The medication is prescribed by or in consultation with a neurologist, geneticist, or a physician who specializes in the treatment of amyloidosis.

CONDITIONS NOT COVERED

- **Wainua™ (eplontersen subcutaneous injection - AstraZeneca)**

is(are) considered experimental, investigational or unproven for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Concurrent use with other medications indicated for the treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis or transthyretin-mediated amyloidosis-cardiomyopathy (e.g., Amvuttra [vutrisiran subcutaneous injection], Attruby [acoramidis tablets], Onpattro [patisiran intravenous infusion], Tegsedi [inotersen subcutaneous injection], or a tafamidis product.)**
   The requested medication should not be administered in combination with other medications indicated for polyneuropathy of hereditary transthyretin-mediated amyloidosis or transthyretin-mediated amyloidosis-cardiomyopathy. Combination therapy is generally not recommended due to a lack of controlled clinical trial data supporting additive efficacy.

REFERENCES

1. Wainua™ subcutaneous injection [prescribing information]. Wilmington, DE: AstraZeneca; September 2024.
2. Alcantara M, Mezi MM, Baker SK, et al. Canadian guidelines for hereditary transthyretin amyloidosis polyneuropathy management. *Can J Nero Sci.* 2022;49:7-18.
3. Kittleson MM, Maurer MS, Ambardekar AV, et al; on behalf of the American Heart Association Heart Failure and Transplantation Committee of the Council on Clinical Cardiology. AHA scientific statement: cardiac amyloidosis: evolving diagnosis and management. *Circulation.* 2020;142:e7-e22.
4. McDonagh TA, Metra M, Adamo M, et al. 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J.* 2021;42:3599-3726.
5. Lin H, Merkel M, Hale C, Marantz JL. Experience of patisiran with transthyretin stabilizers in patients with hereditary transthyretin-mediated amyloidosis. *Neurodegener Dis Manag*. 2020;10(5):289-300.
6. Coelho T, Ando Y, Benson MD, et al. Design and rationale of the global Phase 3 NEURO-TTransform Study of antisense oligonucleotide AKCEA-TTR-L_{rx} (ION-682884-CS3) in hereditary transthyretin-mediated amyloid polyneuropathy. *Neurol Ther.* 2021;10:375-389.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	01/03/2024
Early Annual Revision	**Polyneuropathy of Hereditary Transthyretin-Mediated Amyloidosis (hATTR):** For diagnosis confirmed by genetic testing, rephrased the term "mutation" to "pathogenic variant." **Conditions Not Covered:** Concurrent use with other medications indicated for the treatment of polyneuropathy of hereditary	12/04/2024

	transthyretin-mediated amyloidosis or transthyretin-mediated amyloidosis-cardiomyopathy (e.g., Amvuttra (vutrisiran subcutaneous injection), Attruby (acoramidis tablets), Onpattro (patisiran intravenous infusion), Tegsedi (inotersen subcutaneous injection), or a Tafamidis Product) was changed to as listed (previously Concomitant Use With Amvuttra (vutrisiran subcutaneous injection), Onpattro (patisiran intravenous infusion), Tegsedi (inotersen subcutaneous injection), or a Tafamidis Product).	