WAINUA® (eplontersen) 45 mg injection for subcutaneous use

AstraZeneca Access 360™

LETTER OF MEDICAL NECESSITY GUIDE FOR WAINUA® (eplontersen)

Payers may require a letter of medical necessity to support coverage for WAINUA. This letter should describe why WAINUA is medically necessary for the individual patient and may reference supporting materials such as medical records, clinical history, peer-reviewed publications, Prescribing Information, or other relevant documentation. The letter may be submitted with a prior authorization (PA) request, included with a claim submission, or provided in response to a payer's request for additional information. It should contain patient-specific details, be written on the prescriber's letterhead, be signed by the prescriber, and be submitted to the payer to support a PA request or claim for WAINUA.

This Sample Letter of Medical Necessity is provided for informational purposes only and does not constitute legal advice or official guidance from payers. The template is offered as a resource when responding to a request from a patient's health benefits company to provide a letter of medical necessity for prescribing AstraZeneca medicine. **It is not intended to influence reimbursement decisions or replace the independent medical judgment of a healthcare provider.**

AstraZeneca makes no representations or guarantees that use of this information will result in coverage or payment for WAINUA, or that any payment received will fully offset provider costs.

INDICATION

WAINUA injection, for subcutaneous use, 45 mg is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **Reduced Serum Vitamin A Levels and Recommended Supplementation** WAINUA leads to a decrease in serum vitamin A levels. Supplement with recommended daily allowance of vitamin A. Refer patient to an ophthalmologist if ocular symptoms suggestive of vitamin A deficiency occur.

ADVERSE REACTIONS

Most common adverse reactions (≥9% in WAINUA-treated patients) were vitamin A decreased (15%) and vomiting (9%).

Please see the US full Prescribing Information for WAINUA, available at www.WAINUApi.com.

You are encouraged to report negative side effects of AstraZeneca prescription drugs by calling 1-800-236-9933.
If you prefer to report these to the FDA, call 1-800-FDA-1088.

[Name, Title]
[Address]
[City, State ZIP Code]
[Phone Number]
[Date]
[Contact Name], [Title], [Name of Health Insurance Plan or PBM]
[Address]
[City, State ZIP Code]

Re: [Letter of Medical Necessity for WAINUA® (eplontersen)]
[Request for Expedited Review Due to Medical Urgency]
Insured: [Name]; Member ID Number: [Insurance ID Number]; Group Number: [Number]
Date(s) of service: [Date(s)]

Dear [Contact Name],
I am a board certified [neurologist and ATTR specialist, cardiologist working with an ATTR specialist, or other] and am writing on behalf of my patient, [Name of Patient], to document the medical necessity of WAINUA® (eplontersen) for the treatment of [patient-specific diagnosis].

Patient Medical Overview
[Name of patient] is a[n] [age]-year-old [gender], born on [MM/DD/YYYY], who requires treatment with WAINUA after being diagnosed with [patient-specific diagnosis], confirmed by [include applicable testing regimen if available/appropriate] on [MM/DD/YYYY].

Medical History (Including Clinical Signs and Symptoms) [see page 3 for additional information]
[Provide relevant diagnosis-specific details, including clinical signs and symptoms and describe the severity of disease of your patient's current presentation and disease progression (eg, patient's medical history) based on your medical opinion. Include specific clinical presentations, relevant patient-specific clinical scenarios demonstrating serious medical need, and previous treatments.]

FDA Approval
WAINUA is FDA-approved for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

Medical Necessity
[If Policy Requires Step Therapy/Trial or Failure of Recommended Therapy]
Your policy requires a step through [preferred therapy per clinical policy]. In my medical opinion, [preferred therapy per clinical policy] is not appropriate for my patient. [Include rationale for ineligibility or failure of step therapies including worsening of signs or symptoms of disease state. If multiple steps are required, include reasons for each treatment.]

[Discuss rationale for using WAINUA. Include your professional opinion of your patient's likely prognosis or disease progression without treatment. Please refer to the list of potential considerations from the Letter of Appeal Guide for WAINUA (US-104806) on page 3.] In my medical opinion, WAINUA is the most appropriate treatment for [Name of Patient] with [patient-specific diagnosis], based on its demonstrated clinical efficacy and safety profile.

For Patients Transitioning to WAINUA (if relevant) [see page 4 for additional information]
[Provide treatment rationale for transitioning your patient from an existing therapy to WAINUA.]

Treatment Plan
[Include expected treatment plan including dosing. If applicable you may also want to include direction relevant to administration methodology and/or continued use of prior treatments.]

Summary
Based on the information outlined above, WAINUA is medically necessary for the treatment of this patient. For your convenience, I am enclosing [add list of enclosures (eg, confirmatory genetic testing results and other patient chart notes].

Please contact me at [Phone Number] if you have any questions or require additional information to facilitate prompt approval of WAINUA. Thank you for your timely consideration of this request.

Sincerely,
[Provider's Name]
[Provider's Identification Number]
[Provider's Practice Name]
[Provider's Phone Number]
[Provider's Fax Number]
[Provider's Email]

[Enclosures]
[Supporting clinical documentation. Examples include confirmatory genetic testing results and other patient chart notes, progress notes, clinical trials, guidelines or consensus statements, FDA approval letter, other relevant references and publications regarding prescribed medicine, etc.]
[Consider including Indication and Important Safety Information for WAINUA]
[Consider including full Prescribing Information, including Patient Information, for WAINUA]

INFORMATION PAYERS COMMONLY REQUEST

MEDICAL HISTORY TO CONSIDER INCLUDING, AS APPROPRIATE:

- Genetic confirmation of hATTR, including documentation of a pathogenic *TTR* gene mutation (specify mutation and test date)[1]
- Clinical diagnosis of hATTR-PN, established by a neurologist or physician specialized in the treatment and management of amyloidosis
- Documented ATTR-related neurologic manifestations consistent with hATTR-PN, including sensory, motor, and/or autonomic involvement, as demonstrated by*[,2-6]:
  - Sensory loss
  - Muscle weakness
  - Neuropathic pain or paresthesia
  - Impaired coordination or balance
  - Orthostatic hypotension or syncope
  - Gastrointestinal dysmotility (early satiety, nausea, diarrhea, constipation, alternating bowel habits)
  - Genitourinary dysfunction (urinary retention or incontinence, erectile dysfunction)
  - Weight loss or anorexia
  - Abnormal sweating
- Documented ATTR-related red flag symptoms (eg, carpel tunnel syndrome)[5]
- Functional limitations and impact on activities of daily living attributable to hATTR-PN, including effects on ambulation, balance, manual dexterity, self-care, or occupational functioning[7,8]
- Baseline neurologic disease severity and functional status, documented using one or more validated measures such as[1,9]:
  - Polyneuropathy Disability (PND) score
  - Familial Amyloid Polyneuropathy (FAP) stage
  - Neuropathy Impairment Score (NIS)
- Evidence of disease progression or ongoing neurologic impairment, demonstrated by worsening symptoms, functional decline, or deterioration in validated severity or impairment measures[10]
- Prior or current ATTR-directed therapies, with documentation of treatment duration, clinical response, and reason for transition or discontinuation, if applicable
- Relevant comorbid conditions and concomitant medications that may impact neurologic function or overall disease management
- Contraindications, hypersensitivity, or precautions to agents used in the treatment of hATTR-PN
- No history of liver transplantation

*List is not all inclusive of hATTR clinical signs and symptoms.
ATTR=transthyretin-mediated amyloidosis; hATTR=hereditary transthyretin-mediated amyloidosis; hATTR-PN=hereditary transthyretin-mediated amyloid polyneuropathy; TTR=transthyretin.

POSSIBLE TREATMENT RATIONALE FOR TRANSITIONING PATIENTS TO WAINUA® (eplontersen)

- If you are prescribing WAINUA for a patient transitioning from an alternative therapy, you may want to include additional information specific to the transition plan and rationale. Things to consider may include:
  - Details regarding the alternative therapy including name, dosing, time period of use, and outcomes of treatment
  - Professional rationale regarding why transition to WAINUA may be beneficial to this patient (ie, uninterrupted treatment, effect on polyneuropathy progression, product features (eg, dosage and administration), concomitant use concerns)

KEY RESOURCES AVAILABLE TO YOU

- The **WAINUA Letter of Medical Necessity:** Download this template to use as a general framework to assist in preparing a document on why WAINUA is medically necessary for the individual patient.
- The **Compendium of hATTR-PN References for WAINUA** provides information about specific scientific data and publications that may provide additional evidence for your appeal letter.
- The **Letter of Appeal Guide for WAINUA** provides guidance on how to appeal a rejection from a patient's insurance company.
- Connect with a **Field Reimbursement Manager (FRM)**—FRMs provide education and support to healthcare provider offices to facilitate patient access to their prescribed AstraZeneca medications.
- The **Access and Reimbursement Guide** is a resource that provides education and support about the access and reimbursement process.
- The **WAINUA Full Prescribing Information** provides details and directions on how to prescribe WAINUA and pertinent efficacy and safety data.
- The **Free Limited Supply (FLS) Request** provides a free, short-term supply of WAINUA for eligible patients who are denied immediate access or are awaiting insurance coverage determination. Please note that FLS is a temporary program and does not replace existing affordability programs that may be more appropriate for long-term access barriers.

For additional access resources, please see AstraZeneca Access 360's Forms and Resources or scan the QR code to find the right access and support options for you and your WAINUA patients.

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References: 1. Adams D, Ando Y, Beirão JM, et al. Expert consensus recommendations to improve diagnosis of ATTR amyloidosis with polyneuropathy. *J Neurol*. 2021;268(6):2109-2122. **2.** Gertz M, Adams D, Ando Y, et al. Avoiding misdiagnosis: expert consensus recommendations for the suspicion and diagnosis of transthyretin amyloidosis for the general practitioner. *BMC Fam Pract*. 2020;21(1):198. **3.** National Institute for Health and Care Excellence. Highly specialised technology evaluation: inotersen for treating hereditary transthyretin-related amyloidosis [ID1242]. 2018. **4.** Nativi-Nicolau JN, Karam C, Khella S, Maurer MS. Screening for ATTR amyloidosis in the clinic: overlapping disorders, misdiagnosis, and multiorgan awareness. *Heart Fail Rev*. 2022;27(3):785-793. **5.** Conceição I, González-Duarte A, Obici L, et al. "Red-flag" symptom clusters in transthyretin familial amyloid polyneuropathy. *J Peripher Nerv Syst*. 2016;21(1):5-9. **6.** Gonzalez-Duarte A, Valdés-Ferrer SI, Cantú-Brito C. Characteristics and natural history of autonomic involvement in hereditary ATTR amyloidosis: a systematic review. *Clin Auton Res*. 2019;29(suppl 1):1-9. **7.** Rintell D, Heath D, Braga Mendendez F, et al. Patient and family experience with transthyretin amyloid cardiomyopathy (ATTR-CM) and polyneuropathy (ATTR-PN) amyloidosis: results of two focus groups. *Orphanet J Rare Dis*. 2021;16(1):70. **8.** Lovley A, Raymond K, Guthrie SD, Pollock M, Sanchorawala V, White MK. Patient-reported burden of hereditary transthyretin amyloidosis on functioning and well-being. *J Patient Rep Outcomes*. 2021;5(1):3. **9.** 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. **10.** Ando Y, Waddington-Cruz M, Sekijima Y, et al. Optimal practices for the management of hereditary transthyretin amyloidosis: real-world experience from Japan, Brazil, and Portugal. *Orphanet J Rare Dis*. 2023;18(1):323.

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