WAINUA® (eplontersen) 45 mg injection for subcutaneous use

AstraZeneca Access 360™

LETTER OF APPEAL GUIDE FOR WAINUA® (eplontersen)

When a payer denies a prior authorization (PA), precertification, or reauthorization request for WAINUA, patients have the right to appeal the decision. If a patient chooses to pursue an appeal, you may support the process by submitting an appeal letter with supporting documentation.

As part of the appeal, payers may request additional information to support coverage for WAINUA following a denial. The appeal letter should describe why WAINUA is medically necessary for the patient and may include supporting documentation. The letter may be submitted either in response to the initial denial or following a payer's request for additional information. It should contain patient-specific details, address the reason for denial, be written on the prescriber's letterhead, and be signed by the prescriber.

This Sample Appeal Letter is provided for informational purposes only and does not constitute legal advice or official guidance from payers. The template is offered as a general framework to assist in preparing an appeal. **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. Attachments to be included with the letter of appeal are original claim form, copy of denial or explanation of benefits, and any other additional supporting documents. If you need additional references, please contact our information center at 1-800-236-9933.

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: [First/Second-Level Appeal for Coverage Denial of WAINUA® (eplontersen)]
[Request for Expedited Review Due to Medical Urgency]
Denial Letter Date: [MM/DD/YYYY]
Denial Reference #/Case ID: [Denial Reference #]
Patient: [Name]
Date of Birth: [MM/DD/YYYY]
Member ID Number: [Insurance ID Number] Group Number: [Insurance Group Number]
Rx Group: [Rx Group Number]

Dear [Contact Name],
I am a board certified [neurologist and ATTR specialist, cardiologist working with an ATTR specialist, or other] writing on behalf of my patient, [Name of Patient], to appeal [Name of Payer]'s decision to deny coverage for WAINUA® (eplontersen), which has been prescribed for [patient-specific diagnosis].

It is my understanding, based on your letter of denial dated [MM/DD/YYYY], that coverage has been denied for the following reason(s): [List the Specific Reason(s) for the Denial as Stated in the Denial Letter]. This letter provides information about my patient's medical history and my treatment rationale.

Reason(s) for Denial and Treatment Rationale [see page 3 for additional information]
[In the appeal letter, you will likely want to address each denial reason stated in the denial letter from the insurance plan. Clearly explain why the reason(s) stated by the insurance plan as a cause for denial of coverage do not preclude use of WAINUA. During the appeal process, it is generally not helpful to provide additional information beyond the specific denial reasons.]

In my medical opinion, WAINUA is the most appropriate treatment for [Name of Patient], a[n] [age]-year-old [gender] 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]. The stated reason(s) for denial include [insert each denial reason and address each reason point by point and provide any supporting documentation, if applicable, for why denial is not appropriate].

Summary and Medical History [see page 4 for additional information]
As stated in my initial authorization request, [Name of Patient] presented with [insert specific clinical presentations and previous treatments, including any relevant patient-specific clinical scenarios demonstrating serious medical need].
For the above reasons, I request that you reverse the coverage determination. Delayed or denied access to WAINUA places [Name of Patient] at risk of [include potential medical implications due to lack of treatment as deemed appropriate].

For your additional information, I am enclosing [list enclosures, such as a copy of the denial letter, supporting clinical documentation, etc]. If you have any questions, please feel free to call me at [physician's telephone number] to discuss. Thank you in advance for your immediate attention to this request.

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

[Enclosures]
[At the bottom of your letter, list the items you have enclosed, which may include things such as the original denial letter, 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]
[Consider including full Prescribing Information, including Patient Information]

TREATMENT RATIONALE TO SUPPORT APPEAL

Below are common reasons your adult patient's PA, precertification, or reauthorization request for WAINUA® (eplontersen) may be denied. In this appeal, you will likely want to address each stated reason for denial and include your clinical justification to demonstrate why the requirement is met or should not apply in this patient's case. You may want to attach supporting references and any additional documentation in your reply in order to further support your request.

1 Denial based on lack of documented indication:

- Consider including information regarding this patient's current diagnosis and information regarding any confirmation of the stated diagnosis through genetic or other medical testing
- Consider documentation if the patient's diagnosis aligns to the FDA-approved indication and if standard diagnostic requirements have been met

2 Denial based on lack of documented genetic or other diagnostic testing:

- Consider including information regarding any confirmation of the stated diagnosis through genetic or other medical testing, including applicable date(s) for the testing as well as information regarding the test result

3 Denial based on preferred/required use of an alternative (step) therapy:

- You may wish to provide evidence to support a professional judgment that the indicated therapy is not an appropriate alternative for your patient:
  - If the patient has previously tried and failed the preferred/required alternative, consider including dates of the previous therapy regimen, a description of the treatment outcome(s) including any negative or ineffective results, and rationale for treatment with WAINUA. You may want to include description of treatment outcome or worsening hATTR-PN as evidence by decreased clinical scoring and/or staging (eg, PND score, FAP stage, and/or NIS before and after treatment).[1,2] Additional information may be found in the suggested chart notes below
  - If you feel that the patient's therapy response or quality or life may be impacted by use of the preferred/required alternative due to differences in approved delivery mechanisms, dosing, or other therapy attributes, you may consider documenting why WAINUA would be your preferred therapy for this patient in your professional opinion (eg, treatment burden, logistical barriers, long-term disease management, shared decision-making)
  - Consider whether alternative therapies require infusion, premedication, or infusion monitoring. If so, consider whether this would be suitable for this patient, including considerations such as limited venous access/infusion-center dependence/visit burden/risk of infusion-related reactions/transportation challenges that may impact your therapy approach for this patient

4 Denial due to concomitant use with another therapy:

- If you feel concomitant use of WAINUA with another prescribed therapy is appropriate for this patient, then you may want to consider including:
  - Details regarding the patient's documented treatment and disease status as seen during concomitant use, including any perceived benefits to treatment outcomes
  - Details regarding WAINUA and/or the other prescribed therapy that support such concomitant use
  - Details of the patient's disease state that may make concomitant use appropriate and/or beneficial (eg, treatment of differing disease spectrums)
- Consider whether the following is appropriate for inclusion: Many patients with hATTR have a mixed phenotype, with features of both PN and cardiomyopathy (CM).[1,3] WAINUA is indicated for hATTR-PN in adults.[4] The patient is on [stabilizer Brand Name®/™ (generic)], which is indicated for ATTR-CM. Note whether cited medication is/is not indicated for the treatment of hATTR-PN*

5 Denial based on non-preferred administration method:

- If you feel that the patient's therapy response or quality of life may be impacted by the product's approved delivery mechanism, you may consider including your professional opinion regarding patient-centered considerations such as treatment burden, logistical barriers, long-term disease management and/or adherence, self-administration concerns)

*The safety and efficacy of WAINUA in combination with TTR stabilizers or other TTR-targeting therapies have not been established in controlled clinical trials. Each medication should be prescribed based on its specific FDA-approved indication and individual patient medical necessity.

FAP=familial amyloid polyneuropathy; FDA=US Food and Drug Administration; hATTR=hereditary transthyretin-mediated amyloidosis; hATTR-CM=cardiomyopathy of hereditary transthyretin-mediated amyloidosis; hATTR-PN=hereditary transthyretin-mediated amyloid polyneuropathy; NIS=neuropathy impairment score; PN=polyneuropathy; PND=polyneuropathy disability.

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*[5-9]:
  - 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, carpal tunnel syndrome)[8]
- 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[10,11]
- Baseline neurologic disease severity and functional status, documented using one or more validated measures such as[1,2]:
  - 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[12]
- 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; TTR=transthyretin.

GENERAL TIPS FOR COMPLETING AN APPEAL LETTER

Familiarize yourself with the payer's appeal process. Each payer has specific requirements for submitting an appeal, so it is important to follow their guidelines when submitting an appeal. Many payers require the use of their own appeal request forms, which are typically available on their website. If a payer-specific form is required, submit it along with your appeal letter. Contact the payer directly with any questions and request written instructions to ensure you are following the correct appeal process.

Timing is critical when submitting an appeal. Review the denial letter carefully to identify submission deadlines and any payer-specific timelines or requirements for appeals.

Expedited reviews may be available in urgent situations. If the situation is medically urgent, the patient may request an expedited appeal, with a decision generally issued within 72 hours. For more information, please visit HealthCare.gov.

Understand the reason for the denial. Carefully review the denial letter to determine the payer's stated reason(s). You may also contact the payer to discuss the denial, which can help identify potential pathways for timely resolution:

- **Denials due to inaccurate or incomplete information:** Review the PA or reauthorization request to identify any missing or incorrect information. Once all required information is accurate and complete, resubmit the PA or reauthorization request
- **Denials based on medical rationale:** Ensure the appeal letter includes clear, specific, and relevant medical information that supports the use of WAINUA in accordance with the payer's criteria. The letter should clearly explain why WAINUA is the most appropriate treatment option for the patient
- **Denials related to step therapy requirements:** Clearly outline the rationale for a step therapy exception. Supporting reasons may include:
    1. The patient has contraindications to the required therapy
    2. The required therapy is expected to be ineffective due to the patient's clinical characteristics
    3. The patient previously tried and did not respond to the required therapy under a different health plan
    4. The required medication is not in the patient's best interest based on medical necessity
    5. The patient is stable on their current therapy, and switching treatments would disrupt continuity of care

Submit all required documentation together and in the specified order. Follow the payer's appeal instructions carefully and include all requested materials at the same time. Documentation may include:

- The payer's appeal form (if required)
- Your appeal letter
- A copy of the payer's denial letter
- Supporting materials such as clinical notes, genetic testing results, or other relevant documentation

Leverage support from Field Reimbursement Managers (FRMs). Dedicated FRMs are available to support healthcare provider offices following a PA denial and can help facilitate patient access to prescribed AstraZeneca therapies. FRMs can assist with:

- Education on payer options for PA resubmission, including peer-to-peer reviews, appeal processes, and applicable timelines
- Review of redacted denial letters or Explanation of Benefits (EOB) statements to provide tailored guidance on next steps and best practices

KEY RESOURCES AVAILABLE TO YOU

- The **WAINUA Sample Appeal Letter**: Download this template to use as a general framework to assist in preparing an appeal.
- 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 **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 **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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AstraZeneca Access 360™

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.** 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. **3.** Planté-Bordeneuve V and Said G. Familial amyloid polyneuropathy. *Lancet Neurol*. 2011;10(12):1086-1097. **4.** WAINUA® (eplontersen) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2026. **5.** 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. **6.** National Institute for Health and Care Excellence. Highly specialised technology evaluation: inotersen for treating hereditary transthyretin-related amyloidosis [ID1242]. 2018. **7.** 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. **8.** 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. **9.** 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. **10.** 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. **11.** 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. **12.** 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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