AstraZeneca

When your patient presents with polyneuropathy in

hATTR

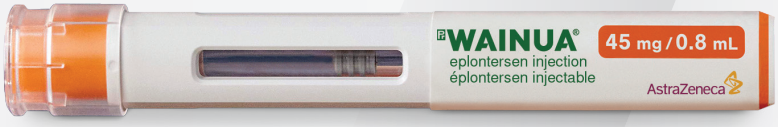
GO WITH

WAINUA®

to treat their PN.

WAINUA (eplontersen injection) is indicated for the treatment of polyneuropathy associated with stage 1 or stage 2 hereditary transthyretin-mediated amyloidosis (hATTR) in adults.[1]

WAINUA is the **FIRST AND ONLY** TTR silencer available for **once-monthly self-injection with an autoinjector**[1,2*†]

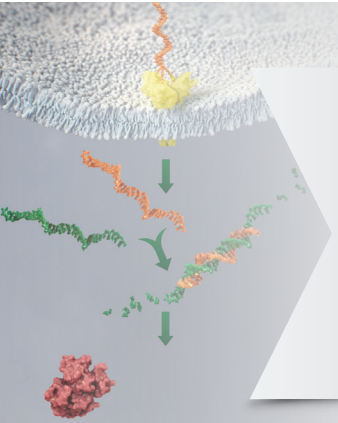


Proper training in subcutaneous injection technique required.

WAINUA®
eplontersen injection

hATTR: hereditary transthyretin–mediated amyloidosis; PN: polyneuropathy; TTR: transthyretin.
* Clinical significance unknown.
† Comparative clinical significance has not been established.

WAINUA® is a TTR silencer that significantly reduces the levels of TTR protein secreted by the liver[1]*



Selectively binds to the TTR mRNA within hepatocytes

Causes the degradation of both mutant and wild-type TTR mRNA

Prevents the synthesis of TTR protein in the liver

Results in significant reductions in the levels of mutated and wild-type TTR protein secreted by the liver into circulation

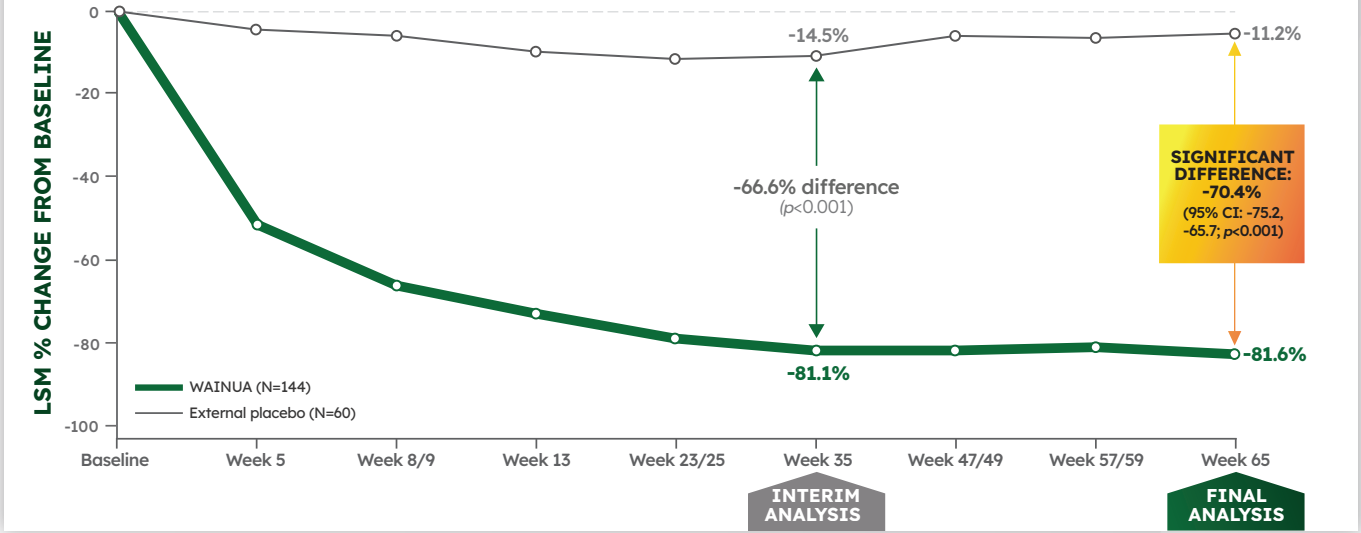
WAINUA was studied in a Phase III, randomized, multicentre, open-label, externally-controlled trial in adult patients with polyneuropathy associated with hATTR (NEURO-TTRansform)[1,3]

NEURO-TTRansform: Patients were randomized 6:1 to the treatment arm, WAINUA (45 mg SC Q4W; N=144), or the reference arm, inotersen (284 mg SC QW to allow for cross-trial comparison of disease progression and treatment responses; N=24), for 34 weeks. Patients in the inotersen group then crossed over to WAINUA and treatment continued. Assessments were based on a comparison of WAINUA vs. external placebo, which was from the inotersen pivotal study, NEURO-TTR (a randomized, double-blind, multicentre clinical trial in adult patients with hATTR-PN). Patients in the external placebo group (N=60) received SC injections of placebo QW. At the interim analysis (Week 35), the primary efficacy endpoint was the change from baseline in the mNIS+7 composite score and the key secondary efficacy endpoint was the change from baseline in the Norfolk QoL-DN questionnaire total score. The pharmacodynamic endpoint was the change from baseline in serum TTR concentration.* The final analysis endpoints were distributed over 2 visits (Week 65 and Week 66), as prespecified in the protocol, and included: change from baseline to Week 66 in the mNIS+7 composite score, change from baseline to Week 66 in the Norfolk QoL-DN total score, and change from baseline to Week 65 in serum TTR concentration.[1,3]*

TTR: transthyretin; mRNA: messenger RNA; hATTR: hereditary transthyretin amyloidosis; SC: subcutaneous; Q4W: every 4 weeks; QW: once weekly; PN: polyneuropathy; mNIS+7: modified Neuropathy Impairment Score+7; Norfolk QoL-DN: Norfolk Quality of Life – Diabetic Neuropathy.
* Clinical significance unknown.

WAINUA® reduced serum TTR concentrations as early as Week 5, with a significant difference in the change from baseline vs. external placebo at Week 35 (when steady state was reached) and through Week 65 ($p<0.001$; pharmacodynamic endpoint)[1,3]*

Change in serum TTR concentration through to 65 weeks[1,3†]



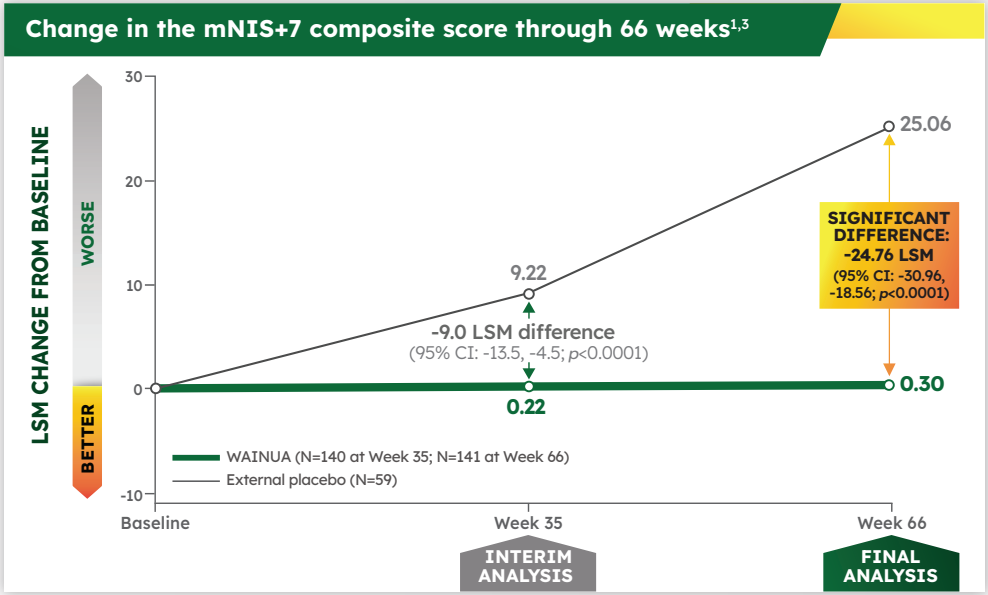
Adapted from the WAINUA Product Monograph and Coelho T, *et al.*[1,3]

† Following baseline, external placebo was assessed at Weeks 5, 8, 13, 23, 35, 47, 59, and 65, while WAINUA was assessed at Weeks 5, 9, 13, 25, 35, 49, 57, and 65.[3]

TTR: transthyretin; LSM: least squares mean; CI: confidence interval.

* Clinical significance unknown.

WAINUA® significantly slowed progression of neuropathy as measured by the mNIS+7 composite score vs. external placebo at Week 35 and through Week 66 (co-primary efficacy endpoint)[1*]



Adapted from the WAINUA Product Monograph and Coelho T, *et al.*[1,3]

The statistical significance of the Week 66 results was not formally tested due to statistically significant results at Week 35.[1]

mNIS+7: modified Neuropathy Impairment Score+7; LSM: least squares mean; CI: confidence interval; SD: standard deviation.
* At baseline, the mean mNIS+7 composite score was 81.3 (SD 43.4).[1]

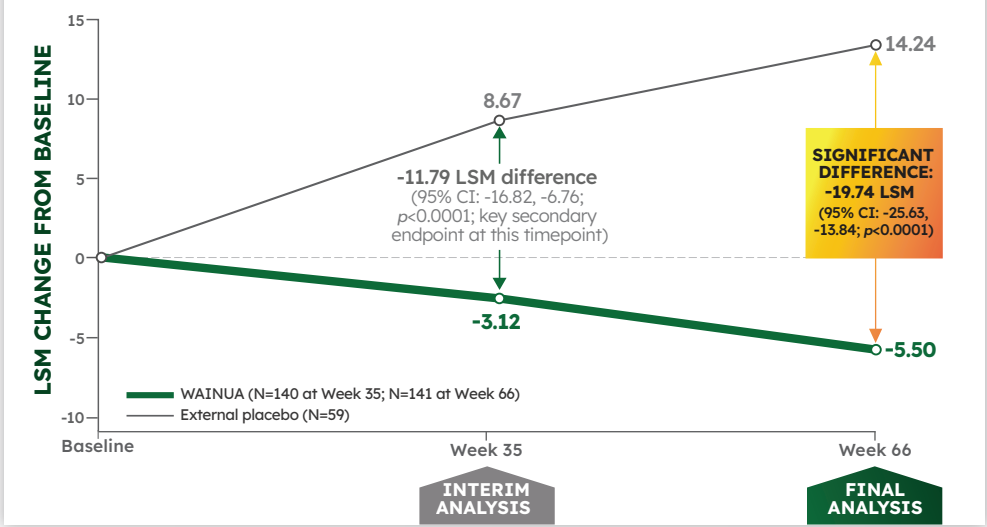
The mNIS+7 is an **objective assessment of neuropathy** with a range of -22.3 to 346.3 points, where higher scores represent a greater severity of disease.[1]

The NIS measures deficits in:[1]
- Cranial nerve function
- Muscle strength
- Reflexes
- Sensations

The Modified +7 composite score measures:[1]
- Heart rate response to deep breathing
- Quantitative sensory testing (touch-pressure and heat-pain)
- Peripheral nerve electrophysiology

WAINUA® significantly improved quality of life as measured by the Norfolk QoL-DN total score vs. external placebo at Week 35 and through Week 66 (co-primary efficacy endpoint)[1]*

Change in the Norfolk QoL-DN total score through 66 weeks[1]



Adapted from the WAINUA Product Monograph.[1]

The statistical significance of the Week 66 results was not formally tested due to statistically significant results at Week 35.[1]

Norfolk QoL-DN: Norfolk Quality of Life – Diabetic Neuropathy; LSM: least squares mean; CI: confidence interval; SD: standard deviation.
* At baseline, the mean Norfolk QoL-DN total score was 44.1 (SD 26.6).[1]

The Norfolk QoL-DN questionnaire is a patient-reported assessment. The version used in the trial had a range from -4 to 136 points, where **higher scores represent greater impairment**.

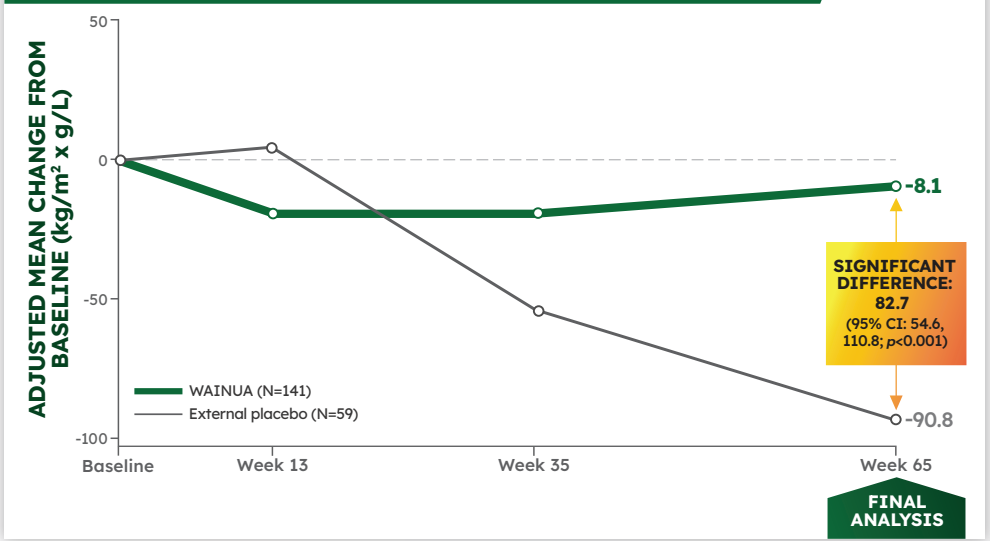
It evaluates the **subjective experience of neuropathy** in the following domains:[1]

- Physical functioning/large fibre neuropathy
- Activities of daily living
- Symptoms
- Small fibre neuropathy
- Autonomic neuropathy

Given the subjective nature of the Norfolk QoL-DN assessment, care should be taken when interpreting the significance of this data, particularly in the context of an open-label trial.[1]

WAINUA® demonstrated statistically significant superiority in nutritional status as measured by the change from baseline in mBMI vs. external placebo at Week 65 ($p<0.001$; select secondary endpoint)[1,3]

Change in mBMI through 65 weeks[3,4]



Adapted from Coelho T, *et al.*[3,4]

Modified body mass index (BMI × serum albumin) is an acceptable method of assessing nutritional status in ATTR.[1]

Higher mBMI scores represent better nutritional status and are considered to be an **indicator of longer survival** in hATTR PN patients.[1]

mBMI: modified body mass index; CI: confidence interval; ATTR: transthyretin-mediated amyloidosis; hATTR: hereditary transthyretin-mediated amyloidosis; PN: polyneuropathy; BMI: body mass index.

WAINUA® was generally well tolerated in NEURO-TTRansform, with a discontinuation rate of 5.6% vs. 3.3% in the external placebo group over 65 weeks[1]

Adverse reactions reported in ≥5% of patients treated with WAINUA up to Week 85[1]	WAINUA N=144 (%)
Eye Disorders	
Vision blurred	6
Cataract	6
Gastrointestinal Disorders	
Vomiting	9
General Disorders and Administration Site Conditions	
Injection site reactions*	6
Metabolism and Nutrition Disorders	
Vitamin A deficiency	12
Renal and Urinary Disorders	
Proteinuria	8

Adapted from the WAINUA Product Monograph.[1]
* Includes injection site erythema and injection site pruritus.

Relevant warnings and precautions:

- Reduced serum vitamin A levels and recommended supplementation
- Driving and operating machinery
- Potential risk of ocular symptoms
- Use in pregnant or breastfeeding women
- Risks related to reproductive health, including teratogenic risk

For more information:

Please consult the Product Monograph at wainua-en.azpm.ca for important information relating to adverse reactions, drug interactions, and dosing information, which has not been discussed in this piece.

The Product Monograph is also available by calling 1-877-404-8277 or emailing ask-medical@astrazeneca.ca.

Demonstrated safety and tolerability profile based on WAINUA exposure in 144 patients with hATTR PN who were randomized to WAINUA and received ≥1 dose of WAINUA for up to 85 weeks.

- 141 patients received ≥6 months of treatment and 137 patients received ≥12 months of treatment.
- The mean duration of treatment was 541 days (range: 57 to 582 days).
- SAEs occurred in 18.8% of patients treated with WAINUA for up to 85 weeks. The most common SAEs (≥1%) were vomiting (3.5%), nausea (1.4%), urinary tract infection (1.4%), and syncope (1.4%).
- The most frequent causally related adverse reaction with WAINUA during treatment was reduced serum vitamin A levels.

hATTR: hereditary transthyretin–mediated amyloidosis; PN: polyneuropathy; SAEs: serious adverse events.

Connect360® Patient Support Program

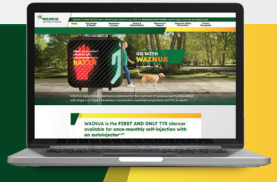
The Connect360 Patient Support Program provides WAINUA® patients with:

- **A dedicated nurse** as a primary point of contact
- **Reimbursement navigation** and financial assistance
- **Injection training** and services
- **Monthly drug delivery** and follow-up
- **Ongoing support** and resources

You can contact Connect360 at: **1-833-733-ATTR (2887)**
(Monday to Friday, 8 am to 8 pm EST) or **support@connect360attr.ca**

Want to know more about WAINUA?

Visit WAINUA.ca for additional information and helpful resources



References: 1. WAINUA® Product Monograph. AstraZeneca Canada Inc. August 26, 2025. **2.** Data on file. AstraZeneca Canada Inc. August 2024. **3.** Coelho T, Marques Jr W, Dasgupta NR, *et al.* Eplontersen for hereditary transthyretin amyloidosis with polyneuropathy. *JAMA*. 2023;330(15):1448–1458. **4.** Supplementary Online Content for: Coelho T, Marques Jr W, Dasgupta NR, *et al.* Eplontersen for hereditary transthyretin amyloidosis with polyneuropathy. *JAMA*. 2023;330(15):1448–1458.

WAINUA® eplontersen injection

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CA-12048E

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REVIEWED BY PAAB