Iowa Medicaid
IOWA HHS

# PDL DRUG REVIEW

**Proprietary Name: Wainua®**
**Common Name: eplontersen**
**PDL Category: Central Nervous System Agents**

| Comparable Products | Preferred Drug List Status |
|---|---|
| Onpattro | Medical |

**Pharmacology/Usage:** Eplontersen, the active ingredient of Wainua®, is a transthyretin-directed antisense oligonucleotide (ASO), covalently linked to a ligand containing three N-acetyl galactosamine (GalNAc) residues to enable delivery of the ASO to hepatocytes. It is an antisense oligonucleotide-GalNAc conjugate that causes degradation of mutant and wild-type transthyretin (TTR) mRNA through binding to the TTR mRNA, which results in a reduction of serum TTR protein and TTR protein deposits in tissues.

**Indication:** For the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

There is no pregnancy category for this medication; however, the risk summary indicates that there are no available data on use in pregnant women to inform a drug-associated risk of adverse developmental outcomes. Wainua® treatment leads to a decrease in serum vitamin A levels, and vitamin A supplementation is advised for patients taking Wainua®. Vitamin A is essential for normal embryofetal development; however, excessive levels of vitamin A are associated with adverse developmental effects. The effect of vitamin A supplementation on the fetus in the setting of a reduction in maternal serum TTR caused by Wainua® administration is not known. The safety and efficacy of use in the pediatric population have not been established.

**Dosage Form:** Solution in a single-dose autoinjector for injection: 45mg/0.8ml.

Remove the autoinjector from the refrigerator 30 minutes prior to injection and allow to warm to room temperature. Do not use other warming methods.

**Recommended Dosage:** The recommended dosage is 45mg administered by subcutaneous injection once monthly. Administer Wainua® as soon as possible after a missed dose. Resume dosing at monthly intervals from the date of the most recently administered dose.

Prior to initiation, train patients and/or caregivers on proper preparation and administration of Wainua®. Administer Wainua® as a subcutaneous injection into the abdomen or upper thigh region. The back of the upper arm can also be used as an injection site if a healthcare provider or caregiver administers the injection.

Dosage adjustments are not required in patients with mild to moderate renal impairment; however, use has not been studied in patients with severe renal impairment or end-stage renal disease. Dose adjustments are not required with mild hepatic impairment; however, use has not been studied in patients with moderate or severe hepatic impairment.

**Drug Interactions:** There are no drug interactions listed with this product.

**Box Warning:** There is no box warning listed with this product.

**Common Adverse Drug Reactions:** *Listed % incidence for adverse drug reactions= reported % incidence for drug (Wainua®). Please note that there was no placebo data in the prescribing information to compare with.* The most frequently reported adverse events included vitamin A decreased (15%), vomiting (9%), proteinuria (8%), injection site reactions (7%), blurred vision (6%), and cataract (6%). Three serious adverse reactions of atrioventricular (AV) heart block (2%) occurred in Wainua®-treated patients, including 1 case of complete AV block.

Wainua® treatment leads to a decrease in serum vitamin A levels. Supplementation at the recommended daily allowance of vitamin A is advised for patients taking Wainua®. Higher doses than the recommended daily allowance of vitamin A should not be given to try to achieve normal serum vitamin A levels during treatment with Wainua®, as serum vitamin A levels do not reflect the total vitamin A in the body. Patients should be referred to an ophthalmologist if they develop ocular symptoms suggestive of vitamin A deficiency (e.g., night blindness, dry eyes).

**Contraindications:** There are no contraindications listed with this product.

**Manufacturer:** AstraZeneca Pharmaceuticals LP

**Analysis:** The efficacy of Wainua® was demonstrated in a randomized, open-label, multicenter trial that included adults with polyneuropathy caused by hereditary transthyretin-mediated amyloidosis (hATTR amyloidosis; Study 1). Patients were randomized in a 6:1 ratio to receive either Wainua® 45mg Q4W (N=144) or inotersen 284mg QW (N=24), respectively, as subcutaneous injections. (Brand name for inotersen is Tegsedi®, used as a reference group, but no information was provided in the prescribing information.) Ninety-seven percent of Wainua®-treated patients and 83% of inotersen-treated patients completed at least 35 weeks of the assigned treatment. Efficacy assessments were based on a comparison of the Wainua® arm of this study with an external placebo group (N=60) in another study composed of a comparable population of adult patients with polyneuropathy caused by hATTR amyloidosis.

The efficacy endpoints were the change from baseline to week 35 in the modified Neuropathy Impairment Scale +7 (mNIS+7) composite score and the change from baseline to week 35 in the Norfolk Quality of Life-Diabetic Neuropathy (QoL-DN) total score. The mNIS+7 is an objective assessment of neuropathy and comprises the neuropathy impairment score (NIS) and Modified +7 composite scores. In the version of the mNIS+7 used in the trial, the NIS objectively measures deficits in cranial nerve function, muscle strength, reflexes, and sensations, and the Modified +7 assesses heart rate response to deep breathing, quantitative sensory testing (touch-pressure and heat-pain), and peripheral nerve electrophysiology. The validated version of the mNIS+7 score used in the trial has a range of -22.3 to 346.3 points, with higher scores representing a greater severity of disease.

The clinical meaningfulness of effects on the mNIS+7 was assessed by the change from baseline to week 35 in Norfolk Quality of Life-Diabetic Neuropathy (QoL-DN) total score. The Norfolk QoL-DN scale is a patient-reported assessment that evaluates the subjective experience of neuropathy in the following domains: physical functioning/large fiber neuropathy, activities of daily living, symptoms, small fiber neuropathy, and autonomic neuropathy. The version of the Norfolk QoL-DN that was used in the trial has a range from -4 to 136 points, with higher scores representing greater impairment.

Treatment with Wainua® resulted in statistically significant improvements in the mNIS+7 and the Norfolk QoL-DN total scores, compared to the external placebo control ($p<0.001$) at week 35. Results are presented in the table below, which was adapted from the prescribing information.

| Endpoint | Baseline, mean | | Change from baseline to week 35, LS mean | | Treatment difference LS Mean | p-value |
|---|---|---|---|---|---|---|
| | Wainua® (N=140) | Placebo (N=59) | Wainua® | Placebo | Wainua® - Placebo | |
| mNIS+7 | 79.6 | 74.1 | 0.2 | 9.2 | -9.0 | <0.001 |
| Norfolk QoL-DN | 43.5 | 48.6 | -3.1 | 8.7 | -11.8 | <0.001 |

**Place in Therapy:** Wainua® is a transthyretin-directed antisense oligonucleotide indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults. Prior to subcutaneous injection, train patients and/or caregivers on proper preparation and administration of Wainua®. The safety and efficacy of Wainua® were assessed in a multicenter, open-label, randomized clinical trial that included adults with polyneuropathy caused by hATTR amyloidosis. Efficacy assessments were based on a comparison of Wainua® with an external placebo group in another study comprised of a comparable population of adults with polyneuropathy caused by hATTR amyloidosis. Results suggested that treatment with Wainua® resulted in statistically significant improvements in the mNIS+7 and the Norfolk QoL-DN total scores compared to the external placebo control (both $p<0.001$) at week 35. Wainua® provides another treatment option for polyneuropathy of hereditary transthyretin-mediated amyloidosis, which can be administered by the patient once monthly and has no box warning.

It is recommended that Wainua® should be non-preferred in order to confirm the appropriate diagnosis and clinical parameters for use.

**PDL Placement:**
☐ **Preferred**
☒ **Non-Preferred**

## References

[1] Wainua [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals; 2023.