## Subject: Onpattro

## Background:

Hereditary transthyretin amyloidosis (TTR amyloidosis; also, hATTR or ATTR) is a slowly progressive condition characterized by the buildup of abnormal deposits of amyloid protein in the body's organs and tissues. TTR amyloidosis (also referred to as familial amyloid polyneuropathy [FAP]) is caused by mutations in the TTR gene.

TTR amyloidosis is the most commonly diagnosed form of hereditary systemic amyloidosis; and the incidence in the U.S. is estimated at 1 in 100,000 people.

Onpattro is an RNA interference (RNAi) therapeutic agent targeting transthyretin for the treatment ofpolyneuropathy of hereditary TTR amyloidosis. Onpattro is the first RNAi therapeutic agent to be approved by the Food and Drug Administration (FDA). The approval was supported by results of the pivotal phase III APOLLO trial, a randomized, placebo-controlled trial evaluating Onpattro for the treatment of TTR amyloidosis.

A total of 224 patients with polyneuropathy caused by hereditary transthyretin-mediated amyloidosis (hATTR amyloidosis) received ONPATTRO in the placebo-controlled and open-label clinical studies, including 186 patients exposed for at least 1 year, 137 patients exposed for at least 2 years, and 52 patients exposed for at least 3 years. In the placebo-controlled study, 148 patients received ONPATTRO or placebo (77) once every 3 weeks for up to 18 months. Baseline demographic and disease characteristics were generally similar between treatment groups.

The primary endpoint was the change from baseline in the modified Neuropathy Impairment Score+7, a composite measure of neuropathy that assesses motor, sensory, and autonomic neuropathy (mNIS+7; range, 0 to 304, with higher scores indicating more impairment) at 18 months. The response to treatment was observed broadly across the Onpattro group, with 74% of the patients having a less than 10-point increase from baseline in the mNIS+7 at 18 months, compared with 14% of the patients in the placebo group. The secondary endpoint of Norfolk Quality of life-diabetic neuropathy (QOL-DN) score was significantly lower with Onpattro than with placebo at 18 months, indicating improved QOL with Onpattro ($P$<0.001). The study reported common adverse events more frequently with Onpattro than with placebo included peripheral edema (30% versus 22%) and infusion-related reactions (19% versus 9%).

**Authorization:** Prior authorization is required for all members enrolled in commercial (HMO, POS, and PPO) products.

## Policy and Coverage Criteria:

Harvard Pilgrim Health Care (HPHC) considers Onpattro for treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis (also called transthyretin-type familial amyloid polyneuropathy [ATTR-FAP]) as medically necessary in adults for a maximum of twelve months of treatment when ALL the following criteria are met:

- The diagnosis is confirmed by detection of a mutation of the TTR gene.

- Patient exhibits clinical manifestations of ATTR-FAP (e.g., amyloid deposition in biopsy specimens, TTR protein variants in serum, progressive peripheral sensory-motor polyneuropathy).
- Patient has not had a prior liver transplant and is not currently on the UNOS liver transplant list
- Documentation of a baseline Polyneuropathy Disability (PND) score of IIIb or lower:
  Stage I: Walking
  Stage II: Impaired walking but without the need for a stick or crutch
  Stage IIIa: Walking with one stick or crutch
  Stage IIIb: Walking with two sticks or crutches

**Continuation of Therapy:**
Continuation of therapy may be considered medically necessary for 12 additional months when documentation confirms a beneficial response to Onpattro therapy and each of the following:

- Documentation of a positive clinical response in terms of at least one of the following: neurologic impairment, motor function, walking or ambulatory status, nutritional status, TTR levels
- Patient has not had a prior liver transplant and is not currently on the UNOS liver transplant list
- Documentation of one of the following Polyneuropathy disability (PND) scores with continuation of coverage based on a PND score of IIIb or lower:
  Stage I: Walking
  Stage II: Impaired walking but without the need for a stick or crutch
  Stage IIIa: Walking with the help of one stick or crutch
  Stage IIIb: Walking with the help of two sticks or crutches
  Stage IV: Confined to a wheelchair or bedridden

**Dosage**
Onpattro should be administered every three weeks at a dosage of 0.3 mg/kg for patients weighing less than 100 kg, and 30 mg every three weeks for member weighing 100 kg or more.

**Exclusions:** Harvard Pilgrim Health Care (HPHC) considers Onpattro as experimental/investigational for all other indications including dosage and frequency beyond Food and Drug Administration (FDA) labeling. Harvard Pilgrim Health Care (HPHC) considers Onpattro not medically necessary for individuals in current treatment with tafamidis, or with alternative RNA interfering therapies, e.g. Tegsedi, for hereditary transthyretin-mediated amyloidosis.

## Coding:

**Codes are listed below for informational purposes only, and do not guarantee member coverage or provider reimbursement. The list may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible.**

| CPT® Code | Description |
|---|---|
| **C9036** | Injection, patisiran, 0.1 mg |

## References:


1. Onpattro [package insert]. Cambridge, MA: Alnylam Pharmaceuticals, Inc.; August 2018.
2. Adams, et al. Patisiran, an RNAi Therapeutic, for Hereditary Transthyretin Amyloidosis. N Engl J Med. 2018 Jul 5; 379(1):11-21.

3. Ando Y, Coelho T, Berk JL, Cruz MW, Ericzon BG, Ikeda S, Lewis WD, Obici L, Planté-Bordeneuve V, Rapezzi C, et al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. Orphanet J Rare Dis. 2013;8:31.
4. Sekijima Y, Yoshida K, Tokuda T, Ikeda S. Familial transthyretin amyloidosis. In: GeneReviews. Seattle (WA): University of Washington, Seattle. 1993-2017. https://www.ncbi.nlm.nih.gov/books/NBK1194/. Accessed 16 January 2019.

**Summary of Changes:**

| Date | Change |
|---|---|
| **2/19** | New policy |

**Approved by Medical Policy Committee: 02/12/19**
**Approved by Clinical Policy Operational Committee: 2/19**
**Policy Effective Date: 04/05/19**
**Initiated: 2/19**