MEDICAL COVERAGE POLICY	
SERVICE:	**Patisiran (Onpattro®)**
Policy Number:	**317**
Effective Date:	**06/01/2025**
Last Review:	**05/12/2025**
Next Review:	**05/12/2026**

Important note: *Unless otherwise indicated, medical policies will apply to all lines of business. Medical necessity as defined by this policy does not ensure the benefit is covered. This medical policy does not replace existing federal or state rules and regulations for the applicable service or supply. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan documents. See the member plan specific benefit plan document for a complete description of plan benefits, exclusions, limitations, and conditions of coverage. In the event of a discrepancy, the plan document always supersedes the information in this policy.*

SERVICE: Patisiran (Onpattro®)

PRIOR AUTHORIZATION: required

POLICY: Please review the plan's EOC (Evidence of Coverage) or Summary Plan Description (SPD) for details.

For Medicare plans, please refer to appropriate Medicare NCD (National Coverage Determination) or LCD (Local Coverage Determination). If there are no applicable NCD or LCD criteria, use the criteria set forth below.

For Medicaid plans, please confirm coverage as outlined in the Texas Medicaid Provider Procedures Manual | TMHP (TMPPM). Texas Mandate HB154 is applicable for Medicaid plans.

Baylor Scott & White Health Plan (BSWHP) may consider patisiran (Onpattro®) medically necessary for the treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis when ALL of the following criteria are met:

Initial requests:

1. Member must have diagnosis of hereditary transthyretin amyloidosis (hATTR) with documented transthyretin (TTR) mutation having any of the following symptoms:
    a. Peripheral neuropathy; **OR**
    b. Autonomic neuropathy (ex. orthostasis, abnormal sweating, dysautonomia [constipation and/or diarrhea, nausea, vomiting, anorexia, early satiety)

    AND
2. Member must have one of the following at baseline:
    a. Polyneuropathy disability (PND) score ≤ IIIb; **OR**
    b. Familial amyloid polyneuropathy (FAP) Stage 1 or 2

    AND
3. Member is ≥18 years of age; **AND**
4. Prescribed by or in consultation with a neurologist or physician who specializes in the treatment of amyloidosis; **AND**
5. Patisiran will be dosed and administered according to FDA approved labeling; **AND**
6. Member does not have any of the following:
    a. Prior liver transplant; **OR**

   b. New York Heart Association heart failure classification >2; **OR**
   c. Concurrent use with other medications indicated for the treatment of hATTR-polyneuropathy or hATTR-cardiomyopathy (eg. vutrisiran [Amvuttra], acoramidi [Attruby], inotersen [Tegsedi], eplontersen [Wainua] or tafamidis [Vyndaqel, Vyndamax]).

Renewal requests:

1. Member meets all initial criteria; **AND**
2. Member shows clinical improvement with one of the following:
   a. Neuropathy Impairment Score (NIS or mNIS+7) of ≥5 and ≤130; **OR**
   b. Norfolk Quality of Life-Diabetic Neuropathy (QoL-DN) Score; **OR**
   c. 10-meter walk test (10-MWT)

   AND
3. Member PND score or FAP disease stage must be the same or better than baseline; **AND**
4. Member has manageable or no side effects

Authorization duration - 6 months

BSWHP considers patisiran for the treatment of all other indications to be experimental and investigational because the effectiveness of this strategy has not been established.

All requests will be reviewed by a clinical pharmacist and medical director.

BACKGROUND:
Amyloidosis refers to a group of protein misfolding disorders that are characterized by abnormal protein fibers accumulating outside of cells and are not soluble in tissues and organs that inhibit normal function. Hereditary transthyretin amyloidosis (TTR amyloidosis) is a slowly progressive condition characterized by the buildup of abnormal deposits of amyloid protein in the body's organs and tissues caused by mutations in the TTR gene.

There are 2 types of transthyretin amyloidosis (ATTR); hereditary (hATTR) and wild-type (ATTRwt); in addition, to ATTR presenting in a predominantly neuropathic phenotype, cardiac phenotype, or mixed phenotype.

The FDA has approved three therapeutic agents specifically for hereditary transthyretin amyloidosis-polyneuropathy (hATTR-PN) which are TTR silencers that inhibit the production of the TTR protein. The therapeutic agents are patisiran (Onpattro), vutrisiran (Amvuttra), eplontersan (Wainua), and inotersen (Tegsedi) which were FDA approved on August 2018, June 2022, December 2023, and October 2018 respectively. Inotersen (Tegsedi) was discontinued September 2024.

A scientific statement from the 2020 American Heart Association (AHA) recommends patients with variant transthyretin amyloidosis (ATTRv) and polyneuropathy should be considered for TTR silencing therapy with patisiran or inotersen; currently, neither is indicated for cardiac variant transthyretin amyloidosis-cardiomyopathy (ATTRv-CM) without polyneuropathy or in wild-type transthyretin amyloidosis-cardiomyopathy (ATTRwt-CM).

On September 13, 2018, the Midwest Comparative Effectiveness Public Advisory Council (CEPAC) conjugated to deliberate and vote on the Institute for Clinical and Economic Review (ICER) report on treatments for hereditary transthyretin-related (hATTR) amyloidosis based on only being treated through supportive measures alone at the time. The evidence highlighted key clinical data and an economic model for patisiran and inotersen. On October 4, 2018, the CEPAC voted unanimously that both patisiran and inotersen represent a similar low-cost long-term value.

APOLLO Phase 2 Trial comprised of nine cohorts that split dosing into cohorts 1-3 receiving 0.01, 0.05, and 0.15 mg/kg patisiran once every 4 weeks, respectively, cohorts 4-5 received 0.3 mg/kg patisiran once every 4 weeks, and cohorts 6-9 received 0.3 mg/kg patisiran once every 3 weeks. For efficacy, the mNIS+7 (modified Neuropathy Impairment Score) showed a median change of -12.0 from baseline at 18 months indicating a substantial improvement in neuropathy function. Patisiran demonstrated >80% reduction in serum transthyretin (TTR) levels. For safety, the most common adverse event observed was infusion-related reactions; including fever, chills, and headaches. However, these reactions were generally mild to moderate and manageable.

APOLLO Phase 3 Trial comprised of 225 (193 completed) patients that were randomized 2:1 to receive 0.3 mg/ kg patisiran or 0.9% saline as the placebo as an intravenous infusion over 80 min once every 3 weeks for 18 months. For efficacy with neuropathy, patients significantly improved with the mNIS+7 score in the patisiran group compared to placebo. The mean change in mNIS+7 score for patisiran at 18 months was -13.8 compared to a worsening of +1.3 in the placebo group (p-value < 0.0001). Patisiran led to a >80% reduction in serum TTR levels. Gait speed in the 10-m walk test showed improvement in 53% patisiran vs.13% of those who received placebo. For safety, the most common adverse events were infusion-related reactions; including fever, chills, headache. However, these reactions were generally mild to moderate and manageable.

HELIOS-A was a phase 3, global, open-label study that enrolled 164 patients comparing the efficacy and safety of vutrisiran (n=122) with an external placebo group (n=77) and patisiran reference group (n=42) as a comparator using dose from APOLLO trial. Patients were randomized 3:1 to subcutaneous vutrisiran 25 mg every 3 months or IV patisiran 0.3 mg/kg every 3 weeks for 18 months. TTR reduction occurred in 81% of vutrisiran group which was considered non-inferior to the 74.7 in patisiran group.

CODES:

Important note: *Due to the wide range of applicable diagnosis codes and potential changes to codes, an inclusive list may not be presented, but the following codes may apply. Inclusion of a code in this section does not guarantee that it will be reimbursed, and patient must meet the criteria set forth in the policy language.*

CPT Codes:	96413: Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug 96415: Chemotherapy administration, intravenous infusion technique; each additional hour (List separately in addition to code for primary procedure)
HCPCS Codes:	J0222: Injection, patisiran, 0.1 mg
ICD10 codes:	
ICD10 Not covered:	

POLICY HISTORY:

Status	Date	Action
Update	8/11/2025	Removed, Medicare NCD/LCD Interqual statement for clarity.

REFERENCES:

The following scientific references were utilized in the formulation of this medical policy. BSWHP will continue to review clinical evidence related to this policy and may modify it at a later date based upon the evolution of the published clinical evidence. Should additional scientific studies become available, and they are not included in the list, please forward the reference(s) to BSWHP so the information can be reviewed by the Medical Coverage Policy Committee (MCPC) and the Quality Improvement Committee (QIC) to determine if a modification of the policy is in order.

1. Adams, David et al. “Efficacy and safety of vutrisiran for patients with hereditary transthyretin-mediated amyloidosis with polyneuropathy: a randomized clinical trial.” *Amyloid : the international journal of experimental and clinical investigation : the official journal of the International Society of Amyloidosis* vol. 30,1 (2023): 1-9. doi:10.1080/13506129.2022.2091985
2. “Institute for Clinical and Economic Review Final Report Highlights Uncertainty in Long-Term Safety and Effectiveness of New Treatments for Hereditary Transthyretin Amyloidosis, Discusses Options for Insurance Coverage Criteria.” *ICER*, 27 Jan. 2021, icer.org/news-insights/press-releases/institute-for-clinical-and-economic-review-final-report-highlights-uncertainty-in-long-term-safety-and-effectiveness-of-new-treatments-for-hereditary-transthyretin-amyloidosis-discusses-options-for-i/.
3. Kittleson MM, Maurer MS, Ambardekar AV, et al; on behalf of the American Heart Association Heart Failure and Transplantation Committee of the Council on Clinical Cardiology. AHA scientific statement: cardiac amyloidosis: evolving diagnosis and management. Circulation. 2020;142:e7-e22.
4. Onpattro® [prescribing information]. Cambridge, MA: Alnylam; January 2023
5. *Patisiran, an Rnai Therapeutic, for Hereditary Transthyretin Amyloidosis | Nejm*, www.nejm.org/doi/full/10.1056/NEJMoa1716153.

6. Suhr, Ole B, et al. "Efficacy and Safety of Patisiran for Familial Amyloidotic Polyneuropathy: A Phase II Multi-Dose Study - Orphanet Journal of Rare Diseases." *BioMed Central*, BioMed Central, 4 Sept. 2015, ojrd.biomedcentral.com/articles/10.1186/s13023-015-0326-6.

***Note**:*
Health Maintenance Organization (HMO) products are offered through Scott and White Health Plan dba Baylor Scott & White Health Plan, and Scott & White Care Plans dba Baylor Scott & White Care Plan. Insured PPO and EPO products are offered through Baylor Scott & White Insurance Company. Scott and White Health Plan dba Baylor Scott & White Health Plan serves as a third-party administrator for self-funded employer-sponsored plans. Baylor Scott & White Care Plan and Baylor Scott & White Insurance Company are wholly owned subsidiaries of Scott and White Health Plan. These companies are referred to collectively in this document as Baylor Scott & White Health Plan.

RightCare STAR Medicaid is offered through Scott and White Health Plan in the Central Texas Medicaid Rural Service Area (MRSA); FirstCare STAR is offered through SHA LLC dba FirstCare Health Plans (FirstCare) in the Lubbock and West MRSAs; and FirstCare CHIP is offered through FirstCare in the Lubbock Service Area.