Harvard Pilgrim Health Care | TUFTS Health Plan

Medical Necessity Guidelines:

Medical Benefit Drug

Amyloidosis Therapies: Amvuttra™ (vutrisiran) and Onpattro® (patisiran)

Effective: April 1, 2026

Guideline Type	☒ Prior Authorization ☐ Non-Formulary ☐ Step-Therapy ☐ Administrative

Public Plans Products

☒ Tufts Health One Care* – A Medicare-Medicaid Plan (a dual eligible product); Fax 617-673-0956

*The MNG applies to Tufts Health One Care members unless a less restrictive LCD or NCD exists.

Senior Products

☒ Tufts Health Plan Senior Care Options (SCO), (a dual-eligible product); Fax 617-673-0956

☒ Tufts Medicare Preferred HMO, (a Medicare Advantage product); Fax 617-673-0956

☒ Tufts Medicare Preferred PPO, (a Medicare Advantage product); Fax 617-673-0956

Note: While you may not be the provider responsible for obtaining prior authorization, as a condition of payment you will need to ensure that prior authorization has been obtained.

Overview

In polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR-PN), amyloid fibrils deposit in the nervous system, leading to pain, muscle weakness, and autonomic dysfunction.

Approval of Onpattro was based on the APOLLO phase 3 trial in adults with polyneuropathy neuropathy impairment score 5 to 130, polyneuropathy disability score ≤3b, Karnofsky performance status at least 60%) caused by hATTR amyloidosis. Patients with prior liver transplant were excluded from the trial. Results were positive for Onpattro and demonstrate that treatment resulted in statistically significant improvements on multiple polyneuropathy scales, including modified Neurologic Impairment Score +7 (primary endpoint), compared to placebo.

Approval of Amvuttra was based on the HELIOS-A phase 3 trial in adults with polyneuropathy (neuropathy impairment score 5 to 130, polyneuropathy disability score ≤3b, Karnofsky performance status at least 60%) caused by hATTR with TTR mutation. Patients with prior liver transplant were excluded from the trial. For this trial, the placebo cohort from the APOLLO trial of Onpattro, was used as an external control group for this trial. Of note, between-group differences in the baseline modified neurologic impairment score between Amvuttra-treated patients and placebo-treated patients exist, and appears to represent that the Amvuttra-treated patients had less severe disease. Results were positive for Amvuttra and demonstrate that treatment resulted in statistically significant improvements on multiple polyneuropathy scales, including modified Neurologic Impairment Score +7 (primary endpoint), compared to placebo.

Approval of Amvuttra for cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) was supported by results of the Phase 3 HELIOS-B trial, in which Amvuttra reduced the risk of all-cause mortality and recurrent cardiovascular events by 28% versus placebo through the 36-month, double-blind study period.

Currently no medication is Food and Drug Administration (FDA)-approved for the treatment of both cardiomyopathy and polyneuropathy of hATTR. Furthermore, there is not reliable evidence demonstrating safety or additive benefit of combining a transthyretin (TTR) silencer (inotersen, eplontersen, patisiran, vutrisiran), with a TTR stabilizer (tafamidis) in someone with cardiomyopathy and polyneuropathy; therefore, combination therapy is not routinely used.

Food and Drug Administration - Approved Indications

Amvuttra (vutrisiran) is a transthyretin-directed small interfering RNA indicated for the treatment of 1) the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults and 2) wild type or hereditary transthyretin amyloid cardiomyopathy for the reduction of cardiovascular mortality, cardiovascular-related hospitalization, and urgent heart failure visits

Onpattro (patisiran) contains a transthyretin-directed small interfering RNA and is indicated for the treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis (ATTR-FAP) in adults.

Clinical Guideline Coverage Criteria

The plan may authorize coverage of Amvuttra or Onpattro when **ALL** of the following criteria are met:

1. Documented diagnosis of hereditary transthyretin-mediated amyloidosis

2. The Member is at least 18 years of age or older

AND

3. Documentation the Member is experiencing progressive peripheral sensory-motor polyneuropathy

AND

4. Prescribed by or in consultation with neurologist or a provider specializing in the treatment of amyloidosis

Cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis

Initial:

The plan may authorize coverage of Amvuttra when all of the following criteria are met:

1. Documented diagnosis of wild type or hereditary (variant) transthyretin amyloid cardiomyopathy, confirmed by one (1) of the following:
    a. Cardiac scintigraphy
    b. Endomyocardial biopsy
    c. Genetic testing
2. History of heart failure (HF), as evidenced by at least one prior hospitalization or current clinical manifestations
3. Patient does not have NYHA Class IV HF
4. Prescribed by or in consultation with a cardiologist
5. Amvuttra will not be used in combination with any other TTR-directed therapy (Vyndaqel, Vyndamax, Attruby, Onpattro, or Wainua)

Reauthorization:

1. Documentation the patient has experienced a positive therapeutic response as evidenced by one (1) of the following:
    a. Improvement in the distance walked on the 6-minute walk test (6MWT) as compared to baseline
    b. Decreased number of cardiovascular-related hospitalizations
    c. Improvement in Kansas City Cardiomyopathy Questionnaire & Overall Summary (KCCQ-OS) score
    d. Clinical improvement in symptoms or slowing of disease progression

Limitations

Initial coverage of Amyloidosis Therapies will be authorized for 12 months. Reauthorization of Amyloidosis Therapies will be provided in 12-month intervals.

Codes

The following code(s) require prior authorization:

Table 1: HCPCS Codes

HCPCS Codes	Description
J0222	Injection, patisiran, 0.1 mg
J0225	Injection, vutrisiran, 1 mg

References

1. Adams D, Gonzalez-Duarte A, O'Riordan WD, et al. Patisiran, an RNAi therapeutic, for hereditary transthyretin amyloidosis. N Engl J Med. 2018;379(1):11-21.
2. Ando Y, Coelho T, Berk JL, et al. Guideline of transthyretin -related hereditary amyloidosis for clinicians. Orphanet Journal of Rare Diseases. 2013;8(31):1-18.
3. Amvuttra (vutrisiran) [package insert]. Cambridge, MA: Alnylam Pharmaceuticals, Inc.; January 2023.
4. Benson MD, Waddington-Cruz M, Berk J, et al. Inotersen treatment for patients with hereditary transthyretin amyloidosis. N Engl J Med. 2018;379(1):22-31.
5. Brannagan T, Wang AK, Coelho T, et al. Open label extension of the phase 3 study NEURO-TTR to assess the long-term efficacy and safety of inotersen in patients with hereditary transthyretin amyloidosis. Neurology. 2018;90(15 Suppl). Abstract P1.324.
6. Lasser KE, Mickle K, Chapman R, et al. Inotersen and patisiran for hereditary transthyretin amyloidosis: effectiveness and value. Evidence report. 2018 August 29. Available from Internet. Accessed 2018 September 12.
7. Onpattro (patisiran) [package insert]. Cambridge, MA: Alnylam Pharmaceuticals, Inc.; January 2023.
8. Suhr OB, Gonzalez-Duarte A, O'Riordan W, et al. Long-term use of patisiran, an investigational RNAi therapeutic, in patients

with hereditary transthyretin-mediated amyloidosis: baseline demographics and interim data from global open label extension study. Presented at 2018 International Symposium on Amyloidosis. Kumamoto, Japan; 2018 March.
9. Fontana M, Berk JL, Gillmore JD, et al. Vutrisiran in Patients with Transthyretin Amyloidosis with Cardiomyopathy. N Engl J Med 2025; 392:33

Approval And Revision History

September 13, 2022: Reviewed by Pharmacy and Therapeutics Committee (P&T)

Subsequent endorsement date(s) and changes made:

- September 21, 2022: Reviewed by the Medical Policy Approval Committee (MPAC).
- December 22, 2022: Administrative update: Amvuttra code J0225 added, effective January 1, 2023
- September 12, 2023: Administrative update to separate out age and diagnosis requirements. Removed the Limitation "Any indications other than FDA-approved indications are considered experimental or investigational and will not be approved by the health plan." (effective 10/1/23).
- November 2023: Administrative Updates: Rebranded from Tufts Health Unify to Tufts Health One Care for 2024 and administrative update in support of calendar year 2024 Medicare Advantage and PDP Final Rule.
- August 13, 2024: No changes (eff 12/1/24).
- September 2024: Joint Medical Policy and Health Care Services UM Committee review (eff 10/1/24).
- June 2025: Administrative update to remove Harvard Pilgrim Health Care Stride Medicare Advantage from the Medical Necessity Guideline template
- December 9, 2025: No changes (eff 1/1/26)
- December 2025: Joint Medical Policy and Health Care Services UM Committee review (effective 1/1/26)
- March 10, 2026: Added coverage criteria for Amvuttra expanded indication for cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (effective 4/1)
- March 2026: Joint Medical Policy and Health Care Services UM Committee review

Background, Product and Disclaimer Information

Point32Health prior authorization criteria to be applied to Medicare Advantage plan members is based on guidance from Medicare laws, National Coverage Determinations (NCDs) or Local Coverage Determinations (LCDs). When no guidance is provided, Point32Health uses clinical practice guidance published by relevant medical societies, relevant medical literature, Food and Drug Administration (FDA)-approved package labeling, and drug compendia to develop prior authorization criteria to apply to Medicare Advantage plan members. Medications that require prior authorization generally meet one or more of the following criteria: Drug product has the potential to be used for cosmetic purposes; drug product is not considered as first-line treatment by medically accepted practice guidelines, evidence to support the safety and efficacy of a drug product is poor, or drug product has the potential to be used for indications outside of the indications approved by the FDA. Prior authorization and use of the coverage criteria within this Medical Necessity Guideline will ensure drug therapy is medically necessary, clinically appropriate, and aligns with evidence-based guidelines. We revise and update Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests revisions.

Treating providers are solely responsible for the medical advice and treatment of Members. The use of this guideline is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to eligibility and benefits on the date of service, coordination of benefits, referral/authorization, utilization management guidelines when applicable, and adherence to plan policies, plan procedures, and claims editing logic.