Harvard Pilgrim Health Care | TUFTS Health Plan

Medical Necessity Guidelines:
Medical Benefit Drugs

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

Effective: September 15, 2026

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

Applies to:

Commercial Products

☒ Harvard Pilgrim Health Care Commercial products; Fax 617-673-0988

☒ Tufts Health Plan Commercial products; Fax 617-673-0988

Public Plans Products

☒ Tufts Health Direct – A Massachusetts Qualified Health Plan (QHP) (a commercial product); Fax 617-673-0988

☐ Tufts Health Together – MassHealth Accountable Care Partnership Plans; Fax 617-673-0939

☒ Tufts Health RITogether – A Rhode Island Medicaid Plan; Fax 617-673-0939

☐ 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

Food and Drug Administration - Approved Indications

Amvuttra (vutrisiran) is a transthyretin-directed small interfering RNA indicated for the treatment of:

- the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults
- the cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis in adults to reduce cardiovascular mortality, cardiovascular hospitalizations 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 in adults.

Clinical Guideline Coverage Criteria

Amvuttra

The plan may authorize coverage of Amvuttra (vutrisiran) for Members when **ALL** the following criteria are met:

Polyneuropathy of hereditary transthyretin-mediated amyloidosis

Initial Authorization Criteria

1. Documented diagnosis of hereditary transthyretin-mediated amyloidosis with polyneuropathy

AND

2. Documentation in the patient's medical record of transthyretin (TTR) mutation

AND

3. Prescribed by or in consultation with a neurologist or physician specializing in the treatment of amyloidosis

AND

4. Documentation of **one (1)** of the following:
    a. Polyneuropathy Disability (PND) score of IIIb or lower
    b. Neuropathy impairment score 5 to 130

c. Karnofsky performance status at least 60%

AND

5. The patient is at least 18 years of age or older

AND

6. Documentation the patient has not had a prior liver transplant

AND

7. Documentation the requested medication will not be used concomitantly with another medication indicated for the management of cardiomyopathy or neuropathy of transthyretin-mediated amyloidosis (e.g., Attruby, Onpattro, Tegsedi, Vyndamax/Vyndagel, Wainua)

Reauthorization Criteria

1. Documented diagnosis of hereditary transthyretin-mediated amyloidosis with polyneuropathy

AND

2. Documentation in the patient's medical record of transthyretin (TTR) mutation

AND

3. The patient is at least 18 years of age or older

AND

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

AND

5. Documentation the requested medication will not be used concomitantly with another medication indicated for the management of cardiomyopathy or neuropathy of transthyretin-mediated amyloidosis (e.g., Attruby, Onpattro, Tegsedi, Vyndamax/Vyndagel, Wainua)

AND

6. Documentation the patient has experienced a positive clinical response as evidenced by improved or stable motor function, neurologic impairment, and quality of life

Cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis

Initial Authorization Criteria

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

AND

2. Documentation demonstrating the absence of monoclonal protein in serum and urine, obtained through laboratory work, to rule out light chain amyloidosis cardiomyopathy

AND

3. Documentation of diagnostic cardiac imaging (e.g., echocardiogram, cardiac magnetic imaging) demonstrating cardiac involvement (e.g., increased thickness of the ventricular wall or interventricular septum)

AND

4. The patient is at least 18 years of age or older

AND

5. Prescribed by a cardiologist

AND

6. Documented history of heart failure, as evidenced by:
    a. At least one previous hospitalization for heart failure
    b. Clinical evidence of heart failure, with signs and symptoms of volume overload or elevated intracardiac pressures warranting diuretic treatment.

AND

7. Documentation the patient does not have New York Heart Association (NYHA) class IV heart failure, or NYHA class III heart failure and is considered high risk (defined as an N-terminal prohormone of B-type natriuretic peptide >3000 ng/L and estimated glomerular filtration rate <45 mL/min/1.73 m2)

AND

8. Documentation the requested medication will not be used concomitantly with another medication indicated for the management of cardiomyopathy or neuropathy of transthyretin-mediated amyloidosis (e.g., Attruby, Onpattro, Tegsedi,

Vyndamax/Vyndagel, Wainua)

Reauthorization Criteria

1. Documented diagnosis of wild type or hereditary (variant) transthyretin amyloid cardiomyopathy

AND

2. Documentation demonstrating the absence of monoclonal protein in serum and urine, obtained through laboratory work, to rule out light chain amyloidosis cardiomyopathy

AND

3. Documentation of diagnostic cardiac imaging (e.g., echocardiogram, cardiac magnetic imaging) demonstrating cardiac involvement (e.g., increased thickness of the ventricular wall or interventricular septum)

AND

4. The patient is at least 18 years of age or older

AND

5. Prescribed by a cardiologist

AND

6. Documented history of heart failure, as evidenced by:
    a. At least one previous hospitalization for heart failure
    b. Clinical evidence of heart failure, with signs and symptoms of volume overload or elevated intracardiac pressures warranting diuretic treatment.

AND

7. Documentation the patient does not have New York Heart Association (NYHA) class IV heart failure, or NYHA class III heart failure and is considered high risk (defined as an N-terminal prohormone of B-type natriuretic peptide >3000 ng/L and estimated glomerular filtration rate <45 mL/min/1.73 m2)

AND

8. Documentation the requested medication will not be used concomitantly with another medication indicated for the management of cardiomyopathy or neuropathy of transthyretin-mediated amyloidosis (e.g., Amvuttra, Onpattro, Tegsedi, Vyndamax/Vyndagel, Wainua)

AND

9. 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

Onpattro

The plan may authorize coverage of Onpattro (patisiran) for Members when **ALL** the following criteria are met:

Polyneuropathy of hereditary transthyretin-mediated amyloidosis

Initial Authorization Criteria

1. Documented diagnosis of hereditary transthyretin-mediated amyloidosis with polyneuropathy

AND

2. Documentation in the patient's medical record of transthyretin (TTR) mutation

AND

3. Prescribed by or in consultation with a neurologist or physician specializing in the treatment of amyloidosis

AND

4. Documentation of **one (1)** of the following:
    a. Polyneuropathy Disability (PND) score of IIIb or lower
    b. Neuropathy impairment score 5 to 130
    c. Karnofsky performance status at least 60%

AND

5. The patient is at least 18 years of age or older

AND

6. Documentation the patient has not had a prior liver transplant

AND

7. Documentation the requested medication will not be used concomitantly with another medication indicated for the management of cardiomyopathy or neuropathy of transthyretin-mediated amyloidosis (e.g., Attruby, Onpattro, Tegsedi, Vyndamax/Vyndagel, Wainua)

Reauthorization Criteria

1. Documented diagnosis of hereditary transthyretin-mediated amyloidosis with polyneuropathy

AND

2. Documentation in the patient's medical record of transthyretin (TTR) mutation

AND

3. The patient is at least 18 years of age or older

AND

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

AND

5. Documentation the requested medication will not be used concomitantly with another medication indicated for the management of cardiomyopathy or neuropathy of transthyretin-mediated amyloidosis (e.g., Attruby, Onpattro, Tegsedi, Vyndamax/Vyndagel, Wainua)

AND

6. Documentation the patient has experienced a positive clinical response as evidenced by improved or stable motor function, neurologic impairment, and quality of life

Limitations

- Initial coverage of Amyloidosis Therapies will be authorized for 12 months. Reauthorization of Amyloidosis Therapies will be provided in 12-month intervals.
- Members new to the plan stable on treatment with Amyloidosis Therapies must meet Initial Authorization criteria if on treatment for less than a year and must meet Reauthorization criteria if on treatment for more than a year.

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.; March 2025.
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.; September 2025.
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: Minor wording changes to make coverage criteria more concise and clearer. Removed the following from Initial Authorization Criteria: “Member exhibits clinical manifestations of ATTR-FAP (transthyretin-type familial amyloid polyneuropathy), e.g., amyloid deposition in biopsy specimens, TTR protein variants in serum, progressive peripheral sensory-motor polyneuropathy.” Updated requirements for demonstration of a clinical benefit in the Reauthorization Criteria. Added “Documentation the requested medication will not be used concomitantly with another medication indicated for the management of cardiomyopathy or neuropathy of transthyretin-mediated amyloidosis (e.g., Tegsedi, Vyndamax)” and removed the Limitation “Combination hereditary amyloidosis product therapy will not be authorized.” Removed the Limitation “Treatment of sensorimotor or autonomic neuropathy not related to hereditary transthyretin- mediated amyloidosis will not be approved.” (effective 12/1/2023).
- August 13, 2024: Added a neuropathy impairment score of 5 to 130 or Karnofsky performance status at least 60% to demonstrate patient has baseline polyneuropathy. Updated Reauthorization criteria to require documentation of a positive clinical response as evidenced by improved or stable motor function, neurologic impairment, and quality of life and removed the requirement that the PND score remains IIIb or lower. Consolidated Tufts Health RITogether, and Commercial Products coverage criteria into one Medical Necessity Guideline (eff 9/1/24).
- June 2025: Administrative update to remove Harvard Pilgrim Health Care Stride Medicare Advantage from the Medical Necessity Guideline template
- September 9, 2025: Added coverage criteria for Amvuttra expanded indication for cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis. (eff 10/1/25)
- September 15, 2026: Administrative updates: Template updated to remove CareLink from the Medical Necessity Guideline template. Template updated from “Tufts Health Together – MassHealth MCO Plan and Accountable Care Partnership Plans” to “Tufts Health Together- MassHealth Accountable Care Partnership Plans.”

Background, Product and Disclaimer Information

Medical Necessity Guidelines are developed to determine coverage for benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. We make coverage decisions using these guidelines, along with the Member’s benefit document, and in coordination with the Member’s physician(s) on a case-by-case basis considering the individual Member's health care needs.

Medical Necessity Guidelines are developed for selected therapeutic or diagnostic services found to be safe and proven effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in our service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. We revise and update Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

For self-insured plans, coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a Medical Necessity Guideline and a self-insured Member’s benefit document, the provisions of the benefit document will govern. For Tufts Health Together (Medicaid), coverage may be available beyond these guidelines for pediatric members under age 21 under the Early and Periodic Screening, Diagnostic and Treatment (EPSDT) benefits of the plan in accordance with 130 CMR 450.140 and 130 CMR 447.000, and with prior authorization.

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.