

Effective: October 1, 2023

Guideline Type	<input checked="" type="checkbox"/> Prior Authorization <input type="checkbox"/> Non-Formulary <input type="checkbox"/> Step-Therapy <input type="checkbox"/> Administrative
<b>Applies to:</b> <input checked="" type="checkbox"/> CarePartners of Connecticut Medicare Advantage HMO plans, Fax 617-673-0956 <input checked="" type="checkbox"/> CarePartners of Connecticut Medicare Advantage PPO plans, 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

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. 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. 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.

## 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.

**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
- AND
2. The Member is at least 18 years of age
- 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

## Limitations

None

## 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.; June 2022.
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.; May 2021.
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. Adams D, et al. HELIOS-A: Results from the Phase 3 Study of Vutrisiran in Patients with Hereditary Transthyretin-Mediated Amyloidosis with Polyneuropathy (S8.003). *Neurology*. 2022 May 03:98 (18 Supplement).
10. Dyck PJB, et al. Development of measures of polyneuropathy impairment in hATTR amyloidosis: From NIS to mNIS + 7. *J Neurol Sci*. 2019;405:116424.
11. Hawkins PN, et al. Evolving landscape in the management of transthyretin amyloidosis. *Ann Med*. 2015;47(8):625–638.

## Approval And Revision History

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

September 21, 2022: Reviewed by the Medical Policy Approval Committee (MPAC).

Subsequent endorsement date(s) and changes made:

- 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 Update in support of calendar year 2024 Medicare Advantage and PDP Final Rule.

## 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 guidelines 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.