Generic Name: N/A

Therapeutic Class or Brand Name: Transthyretin-Mediated Amyloidosis Agents

Applicable Drugs: Amvuttra (vutrisiran), Attruby (acoramidis), Onpattro (patisiran), Vyndamax (tafamidis), Vyndaqel (tafamidis meglumine), Wainua (eplotersen)

Preferred: Onpattro (patisiran), Vyndamax (tafamidis), Vyndaqel (tafamidis meglumine)

Non-preferred: N/A

VSI Excluded Drugs: Amvuttra (vutrisiran), Attruby (acoramidis), Wainua (eplotersen)

Date of Origin: 6/2/2025

Date Last Reviewed / Revised: 10/9/2025

PRIOR AUTHORIZATION CRITERIA

(May be considered medically necessary when criteria I through IV are met)

I. Documented diagnosis of one of the following conditions AND must meet ALL criteria under applicable diagnosis.

A. Polyneuropathy of Hereditary Transthyretin-Mediated Amyloidosis (hATTR-PN)

i. Documentation of ALL the following diagnostic criteria:

1. Transthyretin amyloid deposition confirmed by nuclear scintigraphy OR tissue biopsy.
2. Transthyretin mutation confirmed by genetic testing.
3. Documented symptoms consistent with hATTR polyneuropathy (eg, difficulty walking, weakness in the lower limbs, tingling or pain in the hands or feet).

ii. Documentation of one of the following (1, 2, or 3):

1. Familial amyloid polyneuropathy (FAP) (ie, Coutinho's system) stage 2 or less.
2. Polyneuropathy disability (PND) score IIIb or less.
3. Neuropathy impairment score (NIS) meeting drug-specific criteria (see Table 1).

iii. Treatment must be prescribed by or in consultation with a neurologist.

B. Cardiomyopathy of Wild-type or Hereditary Transthyretin-mediated Amyloidosis (ATTR-CM)

i. Documentation of ALL the following diagnostic criteria:

1. Transthyretin amyloid deposition confirmed by nuclear scintigraphy OR tissue biopsy.
2. Absence of primary (light chain) amyloidosis.

3. For hereditary ATTR-CM: TTR mutation confirmed by genetic testing.

ii. Documented diagnosis of New York Heart Association (NYHA) class I-III heart failure with ALL the following criteria:

1. Clinical history of heart failure with at least one previous hospitalization for heart failure OR clinical evidence of heart failure with symptoms of volume overload or elevated intracardiac pressures requiring diuretic treatment.
2. Evidence of cardiac involvement by transthoracic echocardiography, with an end diastolic interventricular septal wall thickness exceeding 12 millimeters.
3. Baseline N-terminal pro B-type natriuretic peptide (NT-proBNP) AND 6-minute-walk distance (6MWD) meeting drug-specific criteria (see Table 1).

iii. Documented treatment failure or contraindication to a TTR stabilizer (Attruby or Vyndamax/Vyndaqel) before the use of a TTR silencer (Amvuttra).

iv. Treatment must be prescribed by or in consultation with a cardiologist.

II. Minimum age requirement: 18 years old.

III. Request is for a medication with the appropriate FDA labeling, or its use is supported by current clinical practice guidelines. Refer to Table 1 for medication-specific criteria.

IV. Refer to the plan document for the list of preferred products. If the requested agent is not listed as a preferred product, must have documented treatment failure or contraindication to the preferred product(s).

EXCLUSION CRITERIA

- Used in combination with another transthyretin-mediated amyloidosis agent
- Prior liver transplant (except Onpattro)
- hATTR-PN:
  - NYHA heart failure class III or IV
  - Advanced hATTR-PN (FAP Stage 3 or PND Score IV)
- ATTR-CM:
  - NYHA heart failure class IV
  - Prior heart transplant or implanted mechanical cardiac assist device

OTHER CRITERIA

Table 1: Indications, drug-specific criteria, and quantity limits.

Drug	Indications and drug-specific criteria	Quantity limits

Amvuttra	• hATTR-PN
	  ○ NIS score of 5-130
	  ○ Exclusion: For patients with concurrent hATTR-PN and ATTR-CM, only NYHA heart failure class III with NT-proBNP > 3000 pg/mL and eGFR < 45 mL/min/1.73 m2 and class IV are excluded
	• ATTR-CM
	  ○ NT-proBNP ≥ 300 pg/mL
	  ○ 6MWD ≥ 150 meters
	  ○ Exclusion: NYHA heart failure class III with NT-proBNP > 3000 pg/mL and eGFR < 45 mL/min/1.73 m2 and class IV
		One 25 mg syringe every 3 months

Attruby	• ATTR-CM
	  ○ NT-proBNP ≥ 300 pg/mL
	  ○ 6MWD ≥ 150 meters
		112 tablets every 28 days

Onpattro	• hATTR-PN ○ NIS score of 5-130	<100 kg: 0.3 mg/kg every 3 weeks
		≥100 kg: three vials every 3 weeks

Vyndamax	• ATTR-CM
	  ○ NT-proBNP ≥ 600 pg/mL
	  ○ 6MWD ≥ 100 meters
		30 capsules every 30 days

Vyndaqel		120 capsules every 30 days
Wainua	• hATTR-PN ○ NIS score of 10-130	One 45 mg autoinjector every 30 days

QUANTITY / DAYS SUPPLY RESTRICTIONS

- Refer to Table 1

APPROVAL LENGTH

- **Authorization:** 12 months
- **Re-Authorization:** 12 months, with an updated letter of medical necessity or progress notes showing improvement or stabilization with drug treatment and including, but not limited to, the following criteria:
  - hATTR-PN: FAP stage, PND score, NIS score, or symptoms of polyneuropathy.
  - ATTR-CM: 6MWD, symptoms of heart failure, or reduction in cardiovascular hospitalizations.

APPENDIX

Table 2: Familial amyloid polyneuropathy (FAP) or Coutinho's System	
Stage 1	Does not require assistance with ambulation Disease is limited to lower limbs; slight weakness of the extensors of the big toes
Stage 2	Requires assistance with ambulation Motor signs progress in lower limbs with steppage and distal amyotrophies; the muscles of the hands begin to be wasted and weak
Stage 3	Confined to a wheelchair or bedridden Generalized weakness and areflexia

Table 3: Polyneuropathy Disability (PND)	
0	No symptoms
I	Sensory disturbances in extremities but preserved walking capacity
II	Difficulties in walking but without the need for a walking stick
IIIa	One stick or one crutch required for walking
IIIb	Two sticks or two crutches required for walking
IV	Confined to a wheelchair or to bed

Table 4: Neuropathy Impairment Score (NIS)
Cranial nerves (range: 0 to 40)
Muscle weakness (range: 0 to 152)
Sensation loss (finger and toe) (range: 0 to 32)
Decreased muscle stretch reflexes (range: 0 to 20)

REFERENCES

1. Amvuttra. Prescribing information. Alnylam Pharmaceuticals; 2025. Accessed April 22, 2025. https://www.alnylam.com/sites/default/files/pdfs/amvuttra-us-prescribing-information.pdf
2. Attruby. Prescribing information. BridgeBio Pharma; 2024. Accessed April 22, 2025. https://attruby.com/attruby-prescribing-information.pdf
3. Onpattro. Prescribing information. Alnylam Pharmaceuticals; 2023. Accessed January 8, 2025. https://www.alnylam.com/sites/default/files/pdfs/ONPATTRO-Prescribing-Information.pdf

4. Vyndamax and Vyndaqel. Prescribing information. Pfizer Labs; 2023. Accessed April 22, 2025. https://labeling.pfizer.com/ShowLabeling.aspx?id=11685
5. Wainua. Prescribing information. AstraZeneca Pharmaceuticals; 2024. Accessed January 15, 2025. https://den8dhaj6zs0e.cloudfront.net/50fd68b9-106b-4550-b5d0-12b045f8b184/d9f47b27-50ff-4cc5-807e-3f69664872e2/d9f47b27-50ff-4cc5-807e-3f69664872e2_viewable_rendition__v.pdf
6. Coelho T, Marques W, Dasgupta NR, et al. Eplontersen for Hereditary Transthyretin Amyloidosis With Polyneuropathy. JAMA. 2023;330(15):1448–1458.
7. Ando Y, Adams D, Benson MD, et al. Guidelines and new directions in the therapy and monitoring of ATTRv amyloidosis. Amyloid. 2022;29(3):143-155.
8. Adams, David, et al. Efficacy and Safety of Vutrisiran for Patients with Hereditary Transthyretin-Mediated Amyloidosis with Polyneuropathy: A Randomized Clinical Trial. Amyloid: The Journal of Protein Folding Disorders, vol. 30, no. 1, 23 July 2022, pp. 18–26,
9. Kittleson, M, Ruberg, F. et al. 2023 ACC Expert Consensus Decision Pathway on Comprehensive Multidisciplinary Care for the Patient With Cardiac Amyloidosis: A Report of the American College of Cardiology Solution Set Oversight Committee. JACC. 2023 Mar, 81 (11) 1076–1126.
10. Clinical Review Report: Inotersen (Tegsedi): (Akcea Therapeutics, Inc.): Indication: Stage I or II polyneuropathy in adults with hereditary transthyretin-mediated amyloidosis (hATTR) [Internet]. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2020 Jan. Table 31, Comparison of Disease Staging Systems.
11. Dyck PJ, Kratz KM, Lehman KA, Karnes JL, Melton LJ, O'Brien PC, et al. The Rochester diabetic neuropathy study: design, criteria for types of neuropathy, selection bias, and reproducibility of neuropathic tests. Neurology. 1991;41(6):799–807.
12. Kittleson MM, Maurer MS, Ambardekar AV, et al. Cardiac Amyloidosis: Evolving Diagnosis and Management: A Scientific Statement from the American Heart Association. Circulation. 2020;142(1). doi:10.1161/cir.0000000000000792
13. Wasfy JH, Winn AN, Touchette DR, et al. Disease Modifying Therapies for the Treatment of Transthyretin Amyloid Cardiomyopathy; Final Evidence Report. Institute for Clinical and Economic Review, October 21, 2024. https://icer.org/assessment/transthyretinamyloid-cardiomyopathy-2024