POLICY Document for AMVUTTRA (vutrisiran)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 3: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

CAREFIRST: EXCEPTIONS CRITERIA
hATTR DISORDERS

PREFERRED PRODUCTS: ONPATTRO, AMVUTTRA

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the products for the treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis specified in this policy. Coverage for the targeted product is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members who are requesting treatment with the targeted products

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis Products

	Product(s)
Preferred*	• **Amvuttra** (vutrisiran) injection • **Onpattro** (patisiran) injection
Targeted	• **Tegsedi** (inotersen) injection • **Wainua** (eplontersen) injection

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred product.

Coverage for the targeted product is provided when member has a documented inadequate response, contraindication, or intolerable adverse event to all preferred products.

Section 2: Site of Care

Site of Care Criteria
Amvuttra

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated.

Brand Name	Generic Name	Dosage Form
Amvuttra	vutrisiran	subcutaneous

Criteria For Approval For Administration In Outpatient Hospital Setting

This policy provides coverage for provider administered Amvuttra in an outpatient hospital setting for up to 45 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Amvuttra in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

- The member has experienced an adverse reaction to the drug that did not respond to conventional interventions (e.g., acetaminophen, steroids, diphenhydramine, fluids or other pre-medications) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after administration.
- The member is medically unstable (e.g., respiratory, cardiovascular, or renal conditions).
- The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of drug administration AND the patient does not have access to a caregiver.
- Alternative infusion sites (pharmacy, physician office, ambulatory care, etc.) are greater than 30 miles from the member's home.
- The member is less than 14 years of age.

For situations where administration of Amvuttra does not meet the criteria for outpatient hospital administration, coverage for Amvuttra is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

Required Documentation

The following information is necessary to initiate the site of care prior authorization review (where applicable):

- Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after administration
- Medical records supporting the member is medically unstable
- Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver
- Records supporting alternative infusion sites are greater than 30 miles from the member's home
- Medical records supporting the member is new to therapy

Section 3: Clinical Criteria

CAREFIRST: AMVUTTRA

Client Requested: The intent of the criteria is to ensure that patients follow selection elements as established by CareFirst.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

FDA-Approved Indication
Amvuttra is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

All other indications are considered experimental/investigational and not medically necessary.

I. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a neurologist, geneticist, or physician specializing in the treatment of amyloidosis.

II. CRITERIA FOR INITIAL APPROVAL

Polyneuropathy of Hereditary Transthyretin-mediated Amyloidosis
Authorization of 6 months may be granted for treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis (also called transthyretin-type familial amyloid polyneuropathy [ATTR-FAP]) when all of the following criteria are met:

A. Member is at least 18 years of age
B. The diagnosis is confirmed by detection of a mutation of the TTR gene.
C. Member exhibits clinical manifestations of ATTR-FAP (e.g., amyloid deposition in biopsy specimens, TTR protein variants in serum, progressive peripheral sensory-motor polyneuropathy).
D. The member is not a liver transplant recipient.
E. The requested medication will not be used in combination with inotersen (Tegsedi), patisiran (Onpattro) or tafamidis (Vyndaqel, Vyndamax).
F. Amvuttra will be administered as a 25mg dose every 3 months

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for the continued treatment of ATTR-FAP when all of the following criteria are met:
A. The member must have met all initial authorization criteria.
B. The member must have demonstrated a beneficial response to treatment with Amvuttra therapy compared to baseline (e.g., improvement of neuropathy severity and rate of disease progression as demonstrated by the modified Neuropathy Impairment Scale+7 (mNIS+7) composite score, the Norfolk Quality of Life-Diabetic Neuropathy (QoL-DN) total score, polyneuropathy disability (PND) score, FAP disease stage, manual grip strength).

REFERENCES:

SECTION 1

1. Amvuttra [package insert]. Cambridge, MA: Alnylam Pharmaceuticals, Inc.; February 2023.
2. Onpattro [package insert]. Cambridge, MA: Alnylam Pharmaceuticals, Inc.; January 2023.
3. Tegsedi [package insert]. Waltham, MA: Sobi Inc; January 2024.
4. Wainua [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP: September 2024.

SECTION 2

1. Amvuttra [package insert]. Cambridge, MA: Alnylam Pharmaceuticals, Inc; March 2025.