Amvuttra® (vutrisiran)

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the policy is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

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

- Polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults
- Cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis in adults to reduce cardiovascular mortality, cardiovascular hospitalizations and urgent heart failure visits

This policy also informs prescribers of preferred products for the treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

This program applies to the below products specified in this policy when used for an indication that is FDA-approved for the preferred product. Coverage for a non-preferred 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 members requesting treatment with the non-preferred product.

Table 1. Transthyretin-Directed Small Interfering RNA Products

Medication	Generic Name
Preferred Products:	
Onpattro	patisiran

Amvuttra	vutrisiran
Targeted Products:	
Tegsedi	inotersen
Wainua	eplontersen

POLICY

Required Documentation

Submission of the following information is necessary to initiate the prior authorization review:

1. Familial Amyloid Polyneuropathy:
    a. Testing or analysis confirming a mutation of the TTR gene.
    b. Medical records documenting baseline polyneuropathy disability (PND) score or medical records documenting baseline familial amyloid polyneuropathy (FAP) disease stage
    c. Medical record documentation confirming the member demonstrates signs and symptoms of polyneuropathy and an improvement in these signs and symptoms since starting therapy for continuation
2. Cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis:
    a. Biopsy proven disease:
        i. Tissue biopsy confirming the presence of the transthyretin amyloid deposition
        ii. Immunohistochemical analysis, mass spectrometry, tissue staining, or polarized light microscopy results confirming transthyretin precursor proteins
    b. Technetium-labeled bone scintigraphy proven disease:
        i. Scintigraphy tracing results confirming presence of amyloid deposits
        ii. A serum kappa/lambda free light chain ratio, serum protein immunofixation or urine protein immunofixation test result showing the absence of monoclonal proteins
    c. Echocardiography or cardiac magnetic resonance imaging results confirming cardiac involvement
    d. For members with hereditary ATTR-CM: results confirming a mutation of the transthyretin (TTR) gene
    e. Medical records documenting NYHA classification of heart failure
    f. For continuation of therapy: Medical record documentation confirming the member demonstrates a beneficial response to treatment (e.g., improvement in rate of disease progression as demonstrated by distance walked on the 6-minute walk test, the Kansas City Cardiomyopathy Questionnaire-Overall Summary (KCCQ-OS) score, cardiovascular-related hospitalizations, NYHA classification of heart failure, left ventricular stroke volume, NT-proBNP level)

Prescriber Specialties

The requested medication must be prescribed by or in consultation with one of the following:

1. Familial Amyloid Polyneuropathy: neurologist, geneticist, or physician specializing in the treatment of amyloidosis.
2. Cardiomyopathy of wild type or hereditary transthyretin-mediated amyloidosis: cardiologist or physician specializing in the treatment of amyloidosis.

Criteria for Initial Approval

Familial Amyloid Polyneuropathy:

A. Amvuttra may be considered medically necessary for the treatment of familial amyloid polyneuropathy when ALL of the following criteria are met:
   1. Member is 18 years of age or older
   2. Member has a diagnosis of hereditary ATTR amyloidosis with polyneuropathy confirmed by the presence of a TTR gene mutation (e.g., V30M)
   3. Member has a polyneuropathy disability (PND) score ≤ IIIb (see Appendix A) or member has a familial amyloid polyneuropathy (FAP) disease stage ≤ 2 (see Appendix C)
   4. Member has clinical signs and symptoms of polyneuropathy (i.e., weakness, sensory loss, decreased motor strength, decreased gait speed)
   5. Other causes of peripheral neuropathy have been assessed and ruled out (see Appendix B)
   6. Member is receiving Vitamin A supplementation at the recommended daily allowance prior to initiating therapy with the requested drug and will continue to receive for duration of treatment
   7. Member will not be receiving the requested medication in combination with tafamidis (Vyndamax, Vyndaqel), acoramidis (Attruby), patisiran (Onpattro), eplontersen (Wainua) or inotersen (Tegsedi)

Initial approval will be for **9 months**

Cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis:

A. Amvuttra may be considered medically necessary for treatment of cardiomyopathy of wild type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) when ALL of the following criteria are met:
   a. Member does not have NYHA Class IV heart failure or Class III that is considered high risk, defined as an N-terminal prohormone of B-type natriuretic peptide (NT-proBNP) >3000 ng/L and estimated glomerular filtration rate (eGFR) <45 mL/min/1.73 m2 (See Appendix D)
   b. For members with hereditary ATTR-CM, presence of a mutation of the TTR gene was confirmed
   c. The diagnosis is confirmed by one of the following:
      i. The member meets both of the following:
         1. Presence of transthyretin amyloid deposits on analysis of biopsy from cardiac or noncardiac sites (e.g., fat aspirate, gastrointestinal sites, salivary glands, bone marrow)
         2. Presence of transthyretin precursor proteins was confirmed by immunohistochemical analysis, mass spectrometry, tissue staining, or polarized light microscopy
      ii. The member meets both of the following:
         1. Positive ^{99m}technetium-labeled bone scintigraphy tracing
         2. Light chain amyloidosis has been ruled out by a test showing absence of monoclonal proteins (serum kappa/lamda free light chain ratio, serum and urine protein electrophoresis with immunofixation)
   d. Cardiac involvement was confirmed by echocardiography or cardiac magnetic resonance imaging (e.g., end-diastolic interventricular septal wall thickness exceeding 12 mm)
   e. Member exhibits clinical symptoms of cardiomyopathy and heart failure (e.g., dyspnea, fatigue, orthostatic hypotension, syncope, peripheral edema)
   f. The requested medication will not be used in combination with tafamidis (Vyndamax, Vyndaqel), acoramidis (Attruby), patisiran (Onpattro), eplontersen (Wainua) or inotersen (Tegsedi)

Initial approval will be for **12 months**

Continuation of Therapy

Familial Amyloid Polyneuropathy:

Continuation of therapy may be granted for members that meet all initial criteria and have achieved a therapeutic response as evidenced by stabilization or improvement from baseline in polyneuropathy disability (PND), familial amyloid polyneuropathy (FAP) disease stage, or other assessment of disease progression and neuropathy severity (i.e., modified Neuropathy Impairment Scale+7 (mNIS+7) composite score, Norfolk Quality of Life-Diabetic Neuropathy (QoL-DN) total score, neuropathy impairment score (NIS)). Documentation from the medical record must be provided.

Approval will be for **12 months**

Cardiomyopathy of Wild Type or Hereditary Transthyretin-mediated Amyloidosis

Continuation of therapy may be granted for members that meet all initial criteria and have achieved a therapeutic response to treatment with the requested medication therapy (e.g., improvement in rate of disease progression as demonstrated by distance walked on the 6-minute walk test, the Kansas City Cardiomyopathy Questionnaire-Overall Summary [KCCQ-OS] score, cardiovascular-related hospitalizations, NYHA classification of heart failure, left ventricular stroke volume, N-terminal B-type natriuretic peptide [NT-proBNP] level). Documentation from the medical record must be provided.

Approval will be for **12 months**

Other

Amvuttra (vutrisiran) is considered **not medically necessary** for members who do not meet the criteria set forth above.

Dosing and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Quantity Limits Apply

Medication	Standard Limit	FDA Recommended Dosing
Amvuttra (vutrisiran)	1 syringe per 3 months	25 mg administered by a healthcare professional as a subcutaneous injection once every 3 months.

Appendix

A. Polyneuropathy Disability Score (PND)

Stage 0: no impairment
Stage I: sensory disturbances but preserved walking capability
Stage II: impaired walking capability but ability to walk without a stick or crutches
Stage IIIa: walking only with the help of one stick or crutch
Stage IIIb: walking with the help of two sticks or crutches
Stage IV: confined to a wheelchair or bedridden

B. Other Causes of Peripheral Neuropathy

a. Diabetes
b. Glucose Intolerance
c. Vitamin B_{12} deficiency
d. Charcot-Marie-Tooth disease
e. Chemotherapeutic agents (e.g., platins, vincristine, taxanes, lenalidomide, thalidomide)
f. Trauma
g. Vasculitis

h. Autoimmune diseases (e.g., Sjögren's syndrome, lupus, rheumatoid arthritis)
i. Chronic kidney disease
j. Vitamin B_6 toxicity
k. Paraneoplastic syndrome
l. Viral infections (e.g., varicella-zoster, herpes simplex, Lyme disease, West Nile, cytomegalovirus, HIV)

C. Familial Amyloid Polyneuropathy (FAP) Stages

a. Stage 0 – Asymptomatic
b. Stage 1 – Sensory neuropathy
c. Stage 2 – Require assistance for walking
d. Stage 3 – Bedridden or wheelchair bound

D. New York Heart Association (NYHA) Functional Classification

Class	Patient Symptoms
I	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea (shortness of breath)
II	Slight limitation of physical activity. Comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea (shortness of breath)
III	Marked limitation of physical activity. Comfortable at rest. Less than ordinary physical activity causes fatigue, palpitations, or dyspnea (shortness of breath)
IV	Unable to carry on any physical activity without discomfort. Symptoms of heart failure at rest. If any physical activity is undertaken, discomfort increases

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- **J0225 – Injection, vutrisiran (Amvuttra), 1 mg**

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POLICY HISTORY

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