Oscar Clinical Guideline: Amvuttra (vutrisiran) (PG264, Ver. 1)

Amvuttra (vutrisiran)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

ATTR is a rare disease caused by an acquired wild-type variant or an inherited variant that alters the structure and function of TTR. Genetic testing of the TTR gene helps differentiate individuals with the wild-type vs. a genetic variant. Individuals with ATTR generally present with neuropathy or cardiomyopathy or both.

In ATTR-CM, there is an accumulation of amyloid in the body, most commonly the myocardium and peripheral nerves. Individuals may present with heart failure with preserved ejection fraction, right-sided heart failure, atrial fibrillation, aortic stenosis and complete heart block, angina, or cardiogenic shock.

In hATTR-PN, common neurologic manifestations include sensiomotor polyneuropathy, autonomic neuropathy, small-fiber polyneuropathy, and carpal tunnel syndrome.

Guidelines recommend patients should receive disease-modifying pharmacotherapy only within the confines of the clinical trial design. There is no data to support the safety and efficacy of concomitant use of TTR-lowering agents or TTR-stabilizing agents.

Definitions

"6-minute walk test (6MWT)" evaluates patients with cardiopulmonary disease. It measures the distance that a patient can walk on a flat, hard surface in a period of 6 minutes.

"Cardiac biomarkers" are released into the blood when the heart is damaged or stressed. B-type natriuretic peptide and its biologically inert, amino-terminal propeptide counterpart (NT-proBNP), and cardiac troponin (cTn) are elevated in ATTR-CM.

"Cardiac function" measurements may include echocardiographic global longitudinal strain (GLS) or New York Heart Association (NYHA) class. Echocardiographic GLS assesses left ventricular (LV) function. The NYHA functional classification places patients in 1 of 4 categories based on physical activity limitations.

"Estimated glomerular filtration rate (eGFR)" is a measure of how well an individual's kidneys are working. It is based on a blood test and age, sex, and body type.

"Familial Amyloid Polyneuropathy (FAP) and Polyneuropathy disability (PND) disease staging" is a staging system for FAP with higher staging indicating worsening disease.

"Left ventricular (LV) systolic dysfunction" is most commonly assessed by echocardiographic ejection fraction (EF) and is used as a prognostic marker in heart failure. Heart failure with reduced ejection fraction (HFrEF) is LVEF < 40%, midrange is LVEF 40% to 49%, and preserved ejection fraction is LVEF ≥ 50%. Echocardiographic GLS indicates that mild reduced strain is GLS > 12.6%, moderate reduced strain is 8.1% < GLS < 12.5%, and severe reduced strain is GLS ≤ 8.0%.

"Kansas City Cardiomyopathy Questionnaire-Overall Summary (KCCQ-OS)" is a 23-item self-administered questionnaire to measure the individual's perception of their health status, which includes heart failure symptoms, impact on physical and social function, and how their heart failure impacts their quality of life within a 2-week recall period. The Overall Summary Score includes the total symptom, physical function, social limitations and quality of life scores.

"Karnofsky Performance Status (KPS)" refers to a widely used tool for assessing the functional status of adult patients. It is a scale that ranges from 0 to 100, where 100 represents normal functioning with no complaints or evidence of disease, and 0 represents death.

"Neuropathy Impairment Score (NIS)" is the summed scores of standard items of the neuromuscular examination of weakness, reflex loss, and sensation loss. Higher scores indicate increasing neurologic impairment.

"Norfolk Quality of Life-Diabetic Neuropathy (QoL-DN)" assesses quality of life in diabetic polyneuropathy. Increasing total QoL scores indicate worsening.

Clinical Indications

Medical Necessity Criteria for Clinical Review

General Medical Necessity Criteria

The Plan considers Amvuttra (vutrisiran) medically necessary when [ALL, ONE, BOTH, at least NUMBER] of the following criteria are met:

1. The medication is prescribed by or in consultation with a neurologist, geneticist, or physician specializing in the treatment of amyloidosis; *AND*
2. The member is 18 years of age or older; *AND*
3. The member meets ALL of the following criteria:
    a. There is no evidence that the member is a liver transplant recipient; *and*
    b. There is no evidence that the member has an estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m^2 (see Appendix A, Table 1); *AND*
4. Amvuttra (vutrisiran) will not be used in combination with any other drugs approved for the treatment of ATTR (e.g., Attruby [acoramidis], Onpattro [patisiran], Tegsedi [inotersen], Vyndamax [tafamidis], Vydaqel [tafamidis meglumine], or Wainua [eplontersen]); *AND*

5. Amvuttra (vutrisiran) is being prescribed at a dose and frequency that is within FDA approved labeling; *AND*
6. The member meets the applicable Medical Necessity Criteria for Initial Clinical Review or Subsequent Clinical Review listed below.

Medical Necessity Criteria for Initial Clinical Review

Initial Indication-Specific Criteria

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

The Plan considers Amvuttra (vutrisiran) medically necessary when ALL of the following criteria are met:

5. The member meets the above General Medical Necessity Criteria; *AND*
6. The member has a diagnosis of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR); *AND*
7. The member has cardiomyopathy of ATTR supported by ONE of the following:
    a. The member meets BOTH of the following criteria:
        i. Presence of transthyretin amyloid deposits on analysis of biopsy from cardiac or noncardiac sites; *and*
        ii. Presence of transthyretin precursor proteins was confirmed by immunohistochemical analysis, mass spectrometry, tissue staining, or polarized light microscopy; *or*
    b. The member meets BOTH of the following criteria:
        i. Positive technetium-labeled bone scintigraphy tracing; *and*
        ii. Systemic light chain amyloidosis is ruled out by a test showing absence of monoclonal proteins (serum kappa/lambda free light chain ratio, serum protein immunofixation, or urine protein immunofixation); *AND*
8. For members with variant ATTR-CM, presence of a mutation of the TTR gene was confirmed; *AND*
9. The member shows clinical symptoms of cardiomyopathy and heart failure (e.g., dyspnea, fatigue, orthostatic hypotension, syncope, peripheral edema); *AND*
10. The member meets ALL of the following criteria:
    a. No evidence of New York Heart Association (NYHA) Class IV heart failure (see Appendix A, Table 2); *and*
    b. No evidence of polyneuropathy disability (PND) Score IIIa, IIIb, or IV (see Appendix A, Table 3); *AND*
11. The member is unable to use, or has tried and failed Attruby (acoramidis).

If the above prior authorization criteria are met, the requested product will be authorized for up to 12-months.

Polyneuropathy of Hereditary Transthyretin-mediated Amyloidosis (hATTR-PN)

The Plan considers Amvuttra (vutrisiran) medically necessary when ALL of the following criteria are met:

7. The member meets the above General Medical Necessity Criteria; *AND*
8. The member has a diagnosis of hereditary transthyretin-mediated amyloidosis (hATTR); *AND*
9. The member has polyneuropathy of hATTR; *AND*
10. The diagnosis is confirmed by detection of a mutation in the TTR gene; *AND*
11. The member shows clinical manifestations of hATTR-PN (e.g., amyloid deposition in biopsy specimens, TTR protein variants in serum, progressive peripheral sensory-motor polyneuropathy); *AND*
12. The member meets ALL of the following criteria:
    a. The member has a peripheral neuropathy impairment score (NIS) of 5 or greater; *and*
    b. The member has a polyneuropathy disability (PND) score of ≤ IIIb; *and*
    c. The member has a Karnofsky Performance Status score of ≥60%.

If the above prior authorization criteria are met, the requested product will be authorized for up to 12-months.

Continued Care

Medical Necessity Criteria for Subsequent Clinical Review

Subsequent Indication-Specific Criteria

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

The Plan considers Amvuttra (vutrisiran) medically necessary when ALL of the following criteria are met:

5. The member meets the above applicable General Medical Necessity Criteria; *AND*
6. The member has experienced a documented improvement in their ATTR-CM compared to baseline indicated by meeting ONE of the following:
    a. Distance walked on the 6-minute walk test (6MWT)
    b. Kansas City Cardiomyopathy Questionnaire-Overall Summary (KCCQ-OS)
    c. Cardiovascular-related hospitalizations
    d. Cardiac function (e.g., NYHA classification of heart failure, left ventricular stroke volume)
    e. Serum cardiac biomarker (e.g., B-type natriuretic peptide, cardiac troponin)
7. There is no recorded evidence of unacceptable toxicity or adverse reactions to Amvuttra (vutrisiran); *AND*
8. Amvuttra (vutrisiran) is being prescribed at a dose and frequency that is within FDA approved labeling.

If the above reauthorization criteria are met, the requested product will be authorized for up to 12-months.

Polyneuropathy of Hereditary Transthyretin-mediated Amyloidosis (hATTR-PN)

Reauthorization for **Amvuttra (vutrisiran)** will be granted if the member has recent (within the last 6 months) clinical chart documentation demonstrating ALL of the following criteria:

5. The member meets the above applicable General Medical Necessity Criteria; *AND*
6. The member has experienced a documented improvement in their hATTR-PN compared to baseline indicated by meeting **ONE** of the following:
    a. Neuropathy severity and rate of disease progression as demonstrated by the Neuropathy Impairment Score (NIS) or the modified Neuropathy Impairment Scale+7 (mNIS+7) composite score; *or*
    b. Improvement in the Norfolk Quality of Life-Diabetic Neuropathy (QoL-DN) total score; *or*
    c. Polyneuropathy disability (PND) score; *or*
    d. FAP disease stage; *or*
    e. Manual grip strength; *AND*
7. There is no recorded evidence of unacceptable toxicity or adverse reactions to Amvuttra (vutrisiran); *AND*
8. Amvuttra (vutrisiran) is being prescribed at a dose and frequency that is within FDA approved labeling.

If the above reauthorization criteria are met, the requested product will be authorized for up to 12-months.

Experimental or Investigational / Not Medically Necessary

Amvuttra (vutrisiran) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

- AL (primary) amyloidosis
- AA (secondary) amyloidosis
- Dialysis-related amyloidosis (beta2M type)
- Sensorimotor or autonomic neuropathy not related to hATTR amyloidosis

Applicable Billing Codes (CPT/HCPCS Codes)

Table 1	
CPT/HCPCS codes considered medically necessary if criteria are met:	
Code	*Description*
J0225	Injection, vutrisiran, 1 mg

Table 2	
ICD-10 diagnosis codes considered medically necessary with Table 1 (CPT/HCPCS) codes if criteria are met:	
Code	*Description*
E85.1	Neuropathic heredofamilial amyloidosis
E85.4	Organ-Limited Amyloidosis
E85.82	Wild-Type Transthyretin-Related (Attr) Amyloidosis
E85.89	Other Amyloidosis
E85.9	Amyloidosis, Unspecified

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Appendix A

Table 1: eGFR Staging

eGFR in mL/min/1.73 m^2	Kidney Function
90 or higher	Normal kidney function (stage 1)
60-89	Mild loss of kidney function (stage 2)
45-59	Moderate kidney function (stage 3a)
30-44	Moderate kidney function (stage 3b)
15-29	Severe kidney damage (stage 4)

eGFR in mL/min/1.73 m^2	Kidney Function
Less than 15	End stage kidney failure (stage 5)

Table 2: New York Heart Association (NYHA) Functional Classification

Class	Individual Symptoms
I	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation or shortness of breath.
II	Slight limitation of physical activity. Comfortable at rest. Ordinary physical activity results in fatigue, palpitation, shortness of breath or chest pain.
III	Marked limitation of physical activity. Comfortable at rest. Less than ordinary activity causes fatigue, palpitation, shortness of breath or chest pain.
IV	Symptoms of heart failure at rest. Any physical activity causes further discomfort.

Table 3: Stages of Familial Amyloid Polyneuropathy For Locomotion

Familial Amyloid Polyneuropathy (FAP) Staging	FAP Description	Polyneuropathy disability (PND) Disease Staging	PND Description
Stage I	The disease is limited to the lower limbs Walking without any help. Slight weakness of the extensors of the big toes	PND I	Sensory disturbances in extremities Preserved walking capacity
Stage II	Motor signs progress in lower limbs with steppage and distal amyotrophies, the muscles of the hands begin to be wasted and weak. The patient is by then obviously handicapped but can still move around, although needing help.	PND II	Difficulties walking but without the need for a walking stick
		PND IIIa	One stick or one crutch required for walking.
		PND IIIb	Two sticks or two crutches required for walking
Stage III	The patient is	PND IV	Patient confined to a

Familial Amyloid Polyneuropathy (FAP) Staging	FAP Description	Polyneuropathy disability (PND) Disease Staging	PND Description
	bedridden or confined to a wheelchair, generalized weakness and areflexia.		wheelchair or a bed

Clinical Guideline Revision / History Information

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