STATE OF IOWA DEPARTMENT OF
Health AND Human
SERVICES

Amvuttra (vutrisiran)
PAM–067

Iowa Medicaid Program:	Prior Authorization	**Effective Date:**	01/01/2023
Revision Number:	1	**Last Rev Date:**	01/19/2024
Reviewed By:	Medicaid Medical Director	**Next Rev Date:**	01/17/2025
Approved By:	Medicaid Clinical Advisory Committee	**Approved Date:**	01/19/2024

Overview

Medication:[1]	vutrisiran
Brand Name:	Amvuttra®
Pharmacologic Category:	Neurology; transthyretin-directed small interfering RNA
FDA-Approved Indication(s):	Treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults
How Supplied:	Single-dose prefilled syringe, 25 mg/0.5 mL
Dosage and Administration:	25 mg via subcutaneous injection once every 3 months
Benefit Category:	Medical

Descriptive Narrative

Hereditary transthyretin-mediated amyloidosis (hATTR amyloidosis) is an autosomal dominant disorder (>120 TTR gene mutations known) that is characterized by the slowly progressive buildup of amyloid protein in the peripheral and central nervous systems, heart, kidneys, eyes, bone, and gastrointestinal tract. Transthyretin (TTR) is a tetrameric protein primarily produced in hepatocytes. The disease is caused by genetic mutations in the TTR gene that lead the tetrameric TTR protein to break into monomeric units that misfold and aggregate as amyloid fibril deposits.

There are three general forms of the disease, although patients can have overlapping symptoms from all three forms. The neuropathic form (hereditary TTR amyloidosis polyneuropathy [hATTR-PN], also known as transthyretin familial amyloid polyneuropathy [TTRFAP]), is defined by the presence of sensorimotor peripheral neuropathy (with symptoms of numbness, pain, and weakness), focal nerve lesions (e.g., carpal tunnel syndrome), autonomic dysfunction (e.g., orthostatic hypotension, gastrointestinal dysfunction), vitreous opacity of the eye, and glaucoma. The leptomeningeal form is defined by the presence of stroke, intracranial hemorrhage, hydrocephalus, ataxia, spastic paralysis, seizures, dementia, psychosis, and vision impairment. The cardiac form is defined by the presence of arrhythmia, cardiomegaly, heart failure, and death.

In hATTR amyloidosis, misfolding of the TTR protein leads to its aggregation and the formation of amyloid fibrils, which interfere with the normal function of affected organ systems, including the peripheral nervous system (hereditary TTR amyloidosis polyneuropathy [hATTR-PN]. [2] Approximately 100 to 2500 individuals are estimated to have hATTR-PN in the United States.[3]

Guidelines

Guideline of transthyretin-related hereditary amyloidosis for clinicians, published in 2013, was written to help physicians better understand transthyretin amyloidosis—and, specifically, familial amyloidotic polyneuropathy—so they can recognize and manage the disease more easily and discuss it with their patients. It includes guidance on making a definitive diagnosis, explains methods for disease staging and evaluation of disease progression, and discusses symptom mitigation and treatment strategies, including liver transplant and several pharmacotherapies that have shown promise in clinical trials. Some of the pharmacotherapies in clinical trials (such as Amvuttra®) have been approved by the FDA since the 2013 publication of these guidelines.[4]

Criteria

Prior authorization is required.

Amvuttra® is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of hereditary transthyretin-mediated amyloidosis (hATTR amyloidosis) with polyneuropathy, as confirmed by:
    a. Presence of a transthyretin (TTR) gene mutation (e.g., V30M); **AND**
    b. Nerve biopsy which is positive for amyloid deposits (or medical justification is provided as to why treatment should be initiated despite a negative biopsy or no biopsy); **AND**
2. Member has clinical signs and symptoms of polyneuropathy (i.e., weakness, sensory loss, decreased motor strength, decreased gait speed); **AND**
3. Member is 18 years of age or older; **AND**
4. Member has not had a prior liver transplant; **AND**
5. Amvuttra® is not prescribed concurrently with Onpattro® or Tegsedi™; **AND**
6. Prescribed by, or in consultation with, a neurologist; **AND**
7. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 25 mg once every 3 months; or
    b. Regimen is supported by clinical practice guidelines. Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Amvuttra® is considered medically necessary for continuation of therapy when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Member is responding positively to therapy as evidenced by clinically significant improvement or stabilization in clinical signs and symptoms of the disease (e.g., motor strength, ambulation, neurological symptom burden, quality of life, activities of daily living); **AND**
3. Amvuttra® is not prescribed concurrently with Onpattro® or Tegsedi™; **AND**
4. Prescribed by, or in consultation with, a neurologist; **AND**
5. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 25 mg once every 3 months; or
    b. Regimen is supported by clinical practice guidelines. Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Approval Duration and Quantity Limits

	Initial Authorization	Subsequent Authorization(s)
Approval Duration	6 months	12 months
Quantity Limits	25 mg every 3 months	25 mg every 3 months

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
J0225	Injection, vutrisiran, 1 mg

ICD-10	Description
E85.1	Neuropathic heredofamilial amyloidosis

NDC	Labeler	Dosage	Pkg Size	Pkg Qty	Units/Pkg
71336-1003-01	Alnylam Pharmaceuticals, Inc.	1 mg	1	EA	25

Compliance

1. Should conflict exist between this policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions

are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[1] Amvuttra® prescribing information (02/2023). Alnylam Pharmaceuticals, Inc.: Cambridge, MA. Available online at: www.amvuttrahcp.com. Accessed December 4, 2023.

[2] Vutrisiran Clinical Review (NDA 215515). U.S. Food and Drug Administration: Center for Drug Evaluation and Research (CDER). Application Number 215515Orig1s000. Review completed June 13, 2022. Available online at www.accessdata.fda.gov/drugsatfda_docs/nda/2022/215515Orig1s000 MedR.pdf. Accessed December 18, 2023.

[3] Schmidt HH, et al. Estimating the global prevalence of transthyretin familial amyloid polyneuropathy. Muscle Nerve. 2018 May;57(5):829-837. Epub 2018 Feb 1. PMID: 29211930; PMCID: PMC5947118.

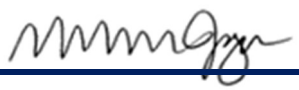
[4] Ando Y, Coelho T, et al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. Orphanet J Rare Dis. 2013 Feb 20;8:31. PMID: 23425518; PMCID: PMC3584981.

Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

Criteria Change History

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
01/19/2024	CAC	Criteria implementation.	1
Signature William (Bill) Jagiello, DO			

CAC = Medicaid Clinical Advisory Committee