

Clinical Policy: Vutrisiran (Amvuttra)

Reference Number: CP.PHAR.550

Effective Date: 06.13.22

Last Review Date: 05.24

Line of Business: Commercial, HIM, Medicaid

[Coding Implications](#)
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See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Vutrisiran (Amvuttra[™]) is a transthyretin-directed small interfering ribonucleic acid (RNA).

FDA Approved Indication(s)

Amvuttra is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis in adults.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation[®] that Amvuttra is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Hereditary Transthyretin-Mediated Amyloidosis (must meet all):

1. Diagnosis of hATTR with polyneuropathy;
2. Prescribed by or in consultation with a neurologist;
3. Age \geq 18 years;
4. Documentation confirms presence of a transthyretin (TTR) mutation;
5. Biopsy is positive for amyloid deposits or medical justification is provided as to why treatment should be initiated despite a negative biopsy or no biopsy;
6. Member has not had a prior liver transplant;
7. Member has not received prior treatment with Onpattro[®], Tegsedi[®], or Wainua[™];
8. Amvuttra is not prescribed concurrently with Onpattro, Tegsedi, or Wainua;
9. Dose does not exceed 25 mg every 3 months.

Approval duration:

Medicaid/HIM – 6 months

Commercial – 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
 - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business:

- CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
- b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Hereditary Transthyretin-Mediated Amyloidosis (must meet all):

1. Member meets one of the following (a or b):
 - a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
 - b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
2. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in any of the following parameters: measures of polyneuropathy (e.g., motor strength, sensation, and reflexes), quality of life, motor function, walking ability (e.g., as measured by timed 10-m walk test), and nutritional status (e.g., as evaluated by modified mass index);
3. Member has not had a prior liver transplant;
4. Amvuttra is not prescribed concurrently with Onpattro, Tegsedi, or Wainua;
5. If request is for a dose increase, new dose does not exceed 25 mg every 3 months.

Approval duration:

Medicaid/HIM – 12 months

Commercial – 6 months or to the member’s renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
 - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
 - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND

criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
hATTR: hereditary transthyretin-mediated

RNA: ribonucleic acid
TTR: transthyretin

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- To confirm amyloidosis, the demonstration of amyloid deposits via tissue biopsy is essential. Deposition of amyloid in the tissue can be demonstrated by Congo red staining of biopsy specimens. With Congo red staining, amyloid deposits show a characteristic green birefringence under polarized light; however, negative biopsy results should not be interpreted as excluding the disease.
- DNA sequencing is usually required for genetic confirmation. Current techniques for performing sequence analysis of TTR, the only gene known to be associated with TTR amyloidosis, detect > 99% of disease-causing mutations.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Polyneuropathy of hATTR	25 mg SC every three months	25 mg/3 months

VI. Product Availability

Single-dose prefilled syringe: 25 mg/0.5 mL

VII. References

1. Amvuttra Prescribing Information. Cambridge, MA: Alnylam Pharmaceuticals, Inc.; February 2023. Available at: <https://www.alnylam.com/sites/default/files/pdfs/amvuttra-us-prescribing-information.pdf>. Accessed February 12, 2024.

2. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). NCT03759379: HELIOS-A: A Study of Vutrisiran (ALN-TTRSC02) in Patients With Hereditary Transthyretin Amyloidosis (hATTR Amyloidosis). Updated July 20, 2021. Available at: <https://clinicaltrials.gov/ct2/show/NCT03759379>. Accessed July 29, 2021.
3. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). NCT04153149: HELIOS-B: A Study to Evaluate Vutrisiran in Patients With Transthyretin Amyloidosis With Cardiomyopathy. Updated July 16, 2021. Available at: <https://clinicaltrials.gov/ct2/show/NCT04153149>. Accessed July 29, 2021.
4. Ando Y, Coelho T, Berk JL, et al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. *Orphanet J Rare Dis*. 2013 Feb 20;8:31.
5. Magrinelli F, Fabrizi GM, Santoro L, et al. Pharmacological treatment for familial amyloid polyneuropathy. *Cochrane Database Syst Rev*. 2020 Apr 20;4(4):CD012395.
6. Adams D, Tournev IL, Taylor MS, et al. Efficacy and safety of vutrisiran for patients with hereditary transthyretin-mediated amyloidosis with polyneuropathy: a randomized clinical trial. *Amyloid*. 2023 Mar; 30 (1): 1-9.
7. Obici L, Polydefkis M, Gonzalez-Duarte A, et al. HELIOS-A: 9-Month Results from the Randomized Treatment Extension Period of Vutrisiran in Patients with Hereditary Transthyretin-Mediated Amyloidosis with Polyneuropathy. Available at: https://capella.alnylam.com/wp-content/uploads/2023/05/HELIOS-A_9-Month-Results-from-the-Randomized-Treatment-Extension-Period-of-Vutrisiran-in-Patients-with-Hereditary-Transthyretin-Mediated-Amyloidosis-with-Polyneuropathy.pdf. Accessed February 12, 2024.
8. Alcantara, M., Mezei, M., Baker, S., et al. Canadian Guidelines for Hereditary Transthyretin Amyloidosis Polyneuropathy Management. *Canadian Journal of Neurological Sciences* 2022. 49 (1): 7-18.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J0225	Injection, vutrisiran, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	08.10.21	11.21
4Q 2022 annual review: RT4: converted PEPP to post-FDA-approved status; clarified Commercial approval duration is 6 months or members renewal date, whichever is longer; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	06.28.22	11.22
Updated HCPCS code: [J0225]	01.06.23	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2023 annual review: no significant changes; references reviewed and updated.	07.10.23	11.23
2Q 2024 annual review: added Wainua to list of drugs that should not have been previously received or prescribed concurrently; references reviewed and updated.	02.12.24	05.24

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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