Medical Drug Clinical Criteria

Subject:	Amvuttra (vutrisiran)		
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Overview

This document addresses the use of Amvuttra (vutrisiran), a small interfering RNA approved by the Food and Drug Administration (FDA) for the treatment of polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis in adults. hATTR amyloidosis was formerly known as familial amyloid polyneuropathy (FAP).

Hereditary transthyretin (hATTR) amyloidosis is a multisystemic, progressive, life-threatening disease characterized by extracellular deposition of amyloid fibrils composed of misfolded transthyretin (TTR), a plasma transport protein produced predominantly by the liver. Amyloid fibrils accumulate in various organs and tissues including the heart, kidney, gastrointestinal tract, and peripheral nerves, resulting in clinical manifestations such as polyneuropathy and cardiomyopathy. Potential symptoms associated with hATTR amyloidosis include but are not limited to muscle weakness, difficulty ambulating, impaired balance, orthostatic hypotension, disturbances in GI mobility, heart failure, arrhythmias, and sudden death due to severe conduction disorders.

Due to the constellation of symptoms and multisystemic nature of the disease, various assessments need to be utilized in an effort to quantify the overall disease burden for each individual with hATTR amyloidosis. Examples of clinical tests include the Neuropathy Impairment Score (NIS) and Polyneuropathy Disability (PND) Score. Amvuttra was studied in individuals with hATTR amyloidosis and mild to moderate polyneuropathy. An example of mild to moderate polyneuropathy status is an individual who is able to ambulate with or without the use of assistance.

The efficacy of Amvuttra was assessed in a randomized, open-label trial in adults with hereditary transthyretin amyloidosis with polyneuropathy. Study participants had a Neuropathy Impairment Score (NIS) of 5-130 (NIS scale ranges from 0-244), a polyneuropathy disability score of IIIb or lower and a TTR mutation confirmed by genotyping. Key exclusion criteria were previous liver transplant, New York Heart Association (NYHA) class III or IV heart failure, severe renal impairment or end-stage renal disease, moderate or severe hepatic impairment and other causes of polyneuropathy unrelated to hATTR amyloidosis. The primary efficacy assessment was reported to favor Amvuttra over placebo, but the clinical trial results are unpublished.

Amvuttra is administered as a subcutaneous injection by a healthcare provider every three months. Treatment with Amvuttra leads to a decrease in serum vitamin A levels. Individuals should be advised to take vitamin A supplementation at the recommended daily allowance while receiving Amvuttra therapy.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Amvuttra (vutrisiran)

Initial requests for Amvuttra (vutrisiran) may be approved if the following criteria are met:

I. Individual has a diagnosis of hereditary transthyretin (hATTR) amyloidosis or familial amyloid polyneuropathy (FAP); **AND**
II. Documentation is provided that individual has a TTR mutation verified by genotyping (NCT 03759379); **AND**

III. Documentation is provided that individual has associated mild to moderate polyneuropathy (NCT 03759379).

Continuation requests for Amvuttra (vutrisiran) may be approved if the following criterion is met:

I. Documentation is provided that there is clinically significant improvement or stabilization in clinical signs and symptoms of disease (including but not limited to improved ambulation, improvement in neurologic symptom burden, improvement in activities of daily living).

Requests for Amvuttra (vutrisiran) may not be approved for the following:

I. Individual has a history of liver transplantation; **OR**
II. Individual has severe renal impairment or end-stage renal disease; **OR**
III. Individual has moderate or severe hepatic impairment; **OR**
IV. Individual has New York Heart Association (NYHA) class III or IV heart failure (NCT 03759379); **OR**
V. Individual has sensorimotor or autonomic neuropathy not related to hATTR amyloidosis (including but not limited to, monoclonal gammopathy, autoimmune disease) (NCT 03759379); **OR**
VI. Individual is using in combination with Onpattro, Tegsedi, Vyndaqel. Vyndamax, or Wainua; **OR**
VII. May not be approved when the above criteria are not met and for all other indications.

Quantity Limits

Amvuttra (vutrisiran) Quantity Limit

Drug	Limit
Amvuttra (vutrisiran) 25 mg/0.5 mL syringe	1 syringe per 3 months

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J0225	Injection, vutrisiran, 1 mg [Amvuttra]

ICD-10 Diagnosis

E85.1	Neuropathic heredofamilial amyloidosis

Document History

Revised: 8/16/2024
Document History:

- 8/16/2024 – Annual Review: Add Wainua to may not be used in combination criteria. Coding Reviewed: No changes.
- 8/18/2023 – Annual Review: Wording and formatting changes. Coding Reviewed: No changes.
- 8/19/2022 – Annual Review: No changes. Coding Reviewed: No changes. Effective 1/1/2023 Added HCPCS J0225. Added ICD-10-CM E85.1. Removed HCPCS J3590, J3490.
- 6/13/2022 – Select Review: Add new clinical criteria and quantity limit for Amvuttra. Coding Reviewed: Added HCPCS J3490, J3590. All diagnoses pend.

References

1. Alnylam Pharmaceuticals. HELIOS-A: A Study of Vutrisiran (ALN-TTRSC02) in Patients With Hereditary Transthyretin Amyloidosis (hATTR Amyloidosis). NLM Identifier: NCT 03759379. Last updated: June 27, 2024. Available at: https://clinicaltrials.gov/ct2/show/NCT03759379. Accessed: July 5, 2024.
2. Ando Y, Coelho T, Berk JL, et. al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. *Orphanet J Rare Dis.* 2013;8(31).
3. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: July 2, 2024.

4. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
5. Gertz MA, Benson MD, Dyck PJ, et. al. Diagnosis, Prognosis, and Therapy of Transthyretin Amyloidosis. *J Am Coll Cardiol*. 2015;66(21):2451-2466.
6. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.