Clinical Policy: Vutrisiran (Amvuttra)

Reference Number: ERX.SPA.450
Effective Date: 06.13.22
Last Review Date: 11.22
Line of Business: Commercial, Medicaid

Revision Log

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 ≥ 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™ or Tegsedi™;
8. Amvuttra is not prescribed concurrently with Onpattro or Tegsedi;
9. Dose does not exceed 25 mg every 3 months.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
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 or Tegsedi;

5. If request is for a dose increase, new dose does not exceed 25 mg every 3 months.
Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 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.; June 2022. Available at: https://www.alnylam.com/sites/default/files/pdfs/amvuttra-us-prescribing-information.pdf. Accessed June 28, 2022.
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.

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; references reviewed and updated.	06.28.22	11.22

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.