Vutrisiran (Amvuttra™)

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the medical policy and a health plan or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

The proposal is to add text/statements in red and to delete text/statements with strikethrough:

POLICY

INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Amvuttra is indicated for the treatment of:

- The polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR-PN) in adults.
- The cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) in adults to reduce cardiovascular mortality, cardiovascular hospitalizations, and urgent heart failure visits.

All other indications are considered experimental/investigational and not medically necessary.

DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
Initial Requests

- For the polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR-PN):
  - Testing or analysis confirming a pathogenic variant ~~mutation~~ in the TTR gene.
  - Medical record documentation demonstrating clinical manifestations of transthyretin-type familial amyloid polyneuropathy [ATTR-FAP] (e.g., amyloid deposition in biopsy specimens, TTR protein variants in serum, progressive peripheral sensory-motor polyneuropathy).
  - Medical record documentation confirming the member demonstrates signs and symptoms of polyneuropathy.
- For the cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM):
  - Chart notes or medical record documentation confirming history of prior hospitalization for heart failure or confirming the member demonstrates clinical symptoms of heart failure at baseline.
  - For biopsy-proven disease:
    - Tissue biopsy from cardiac or noncardiac sites confirming the presence of the transthyretin amyloid deposition.
    - Immunohistochemical analysis, mass spectrometry, tissue staining, or polarized light microscopy results confirming the presence of transthyretin precursor proteins.
  - For technetium-labeled bone scintigraphy proven disease:
    - Scintigraphy tracing results confirming the presence of amyloid deposits.

- Serum kappa/lambda free light chain ratio, serum protein immunofixation, and urine protein immunofixation test results showing the absence of monoclonal proteins.
- For hereditary ATTR-CM: testing or analysis confirming a pathogenic or likely pathogenic variant in the transthyretin (TTR) gene.

~~Medical record documentation confirming the member demonstrates signs and symptoms of polyneuropathy~~
~~Continuation requests: Chart notes or medical record documentation supporting clinical benefit of therapy compared to baseline.~~

Continuation Requests

- For the polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR-PN):
  - Chart notes or medical record documentation supporting clinical benefit of therapy compared to baseline (e.g., improvement of neuropathy severity and rate of disease progression as demonstrated by the modified Neuropathy Impairment Scale+7 (mNIS+7) composite score, the Norfolk Quality of Life-Diabetic Neuropathy (QoL-DN) total score, polyneuropathy disability (PND) score, FAP disease stage, manual grip strength).
- For the cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM):
  - Chart notes or medical record documentation supporting clinical benefit of therapy compared to baseline (e.g., improvement in rate of disease progression as demonstrated by distance walked on the 6-minute walk test, the Kansas City Cardiomyopathy Questionnaire–Overall Summary [KCCQ-OS] score, cardiovascular-related hospitalizations, New York Heart Association [NYHA] classification of heart failure, left ventricular stroke volume, N-terminal B-type natriuretic peptide [NT-proBNP] level).

PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a neurologist, geneticist, cardiologist, or physician specializing in the treatment of amyloidosis.

COVERAGE CRITERIA ~~FOR INITIAL APPROVAL~~

Polyneuropathy of Hereditary Transthyretin-mediated Amyloidosis

Authorization of 12 months may be granted for the treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis (also called transthyretin-type familial amyloid polyneuropathy [ATTR-FAP]) when all of the following criteria are met:

- Member is 18 years of age or older.
- The diagnosis is confirmed by detection of a pathogenic variant ~~mutation~~ in the TTR gene.
- Member exhibits clinical manifestations of ATTR-FAP (e.g., amyloid deposition in biopsy specimens, TTR protein variants in serum, progressive peripheral sensory-motor polyneuropathy).
- ~~The~~ Member is not a liver transplant recipient.
- The requested medication will not be used in combination with patisiran (Onpattro), inotersen (Tegsedi), eplontersen (Wainua), acoramidis (Attruby), tafamidis meglumine (Vyndaqel), or tafamidis (Vyndamax) ~~any other medication approved for the treatment of hereditary transthyretin-mediated amyloidosis (e.g., Onpattro, Tegsedi, Vyndamax, Vyndaqel, Wainua)~~.

Cardiomyopathy of Wild-type or Hereditary Transthyretin-Mediated Amyloidosis

Authorization of 12 months may be granted for the treatment of cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) when all of the following criteria are met:

- Member is 18 years of age or older.
- Member has medical history of heart failure with at least one prior hospitalization for heart failure (not due to arrhythmia or a conduction system disturbance treated with a permanent pacemaker), OR exhibits clinical

symptoms of heart failure (e.g., volume overload, dyspnea, fatigue, orthostatic hypotension, syncope, peripheral edema) at baseline.
- The diagnosis is confirmed by either of the following criteria:
  - Member meets both of the following criteria for biopsy proven disease:
    - Presence of transthyretin amyloid deposits on analysis of biopsy from cardiac or noncardiac sites.
    - Presence of transthyretin precursor proteins was confirmed by immunohistochemical analysis, mass spectrometry, tissue staining, or polarized light microscopy.
  - Member meets both of the following criteria for technetium-labeled bone scintigraphy proven disease:
    - Presence of amyloid deposits confirmed by technetium-labeled bone scintigraphy tracing.
    - Systemic light chain amyloidosis is ruled out by showing the absence of monoclonal proteins by all of the following tests: a) serum kappa/lambda free light chain ratio, b) serum protein immunofixation, and c) urine protein immunofixation.
- For members with hereditary ATTR-CM: the diagnosis is confirmed by detection of a pathogenic or likely pathogenic variant in the TTR gene.
- Member does not have prior or anticipated heart, liver, or other organ transplant or implantation of left-ventricular assist device.
- The requested medication will not be used in combination with patisiran (Onpattro), inotersen (Tegsedi), eplontersen (Wainua), acoramidis (Attruby), tafamidis meglumine (Vyndaqel), or tafamidis (Vyndamax).

CONTINUATION OF THERAPY

Authorization of 12 months may be granted for ~~the~~ continued treatment in members requesting reauthorization for an indication listed in the coverage criteria section ~~IV~~ when all of the following criteria are met:
- Member must ~~have met~~ meet all requirements in the coverage ~~initial authorization~~ criteria.
- ~~Member must have demonstrated a beneficial response to treatment with the requested medication compared to baseline (e.g., improvement of neuropathy severity and rate of disease progression as demonstrated by the modified Neuropathy Impairment Scale+7 (mNIS+7) composite score, the Norfolk Quality of Life-Diabetic Neuropathy (QoL-DN) total score, polyneuropathy disability (PND) score, FAP disease stage, manual grip strength).~~
- For the polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR-PN):
  - Member must have demonstrated a beneficial response to treatment with the requested medication compared to baseline (e.g., improvement of neuropathy severity and rate of disease progression as demonstrated by the modified Neuropathy Impairment Scale+7 (mNIS+7) composite score, the Norfolk Quality of Life-Diabetic Neuropathy (QoL-DN) total score, polyneuropathy disability (PND) score, FAP disease stage, manual grip strength).
- For the cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM):
  - Member must have demonstrated a beneficial response to treatment with the requested medication compared to baseline (e.g., improvement in rate of disease progression as demonstrated by distance walked on the 6-minute walk test, the Kansas City Cardiomyopathy Questionnaire–Overall Summary [KCCQ-OS] score, cardiovascular-related hospitalizations, New York Heart Association [NYHA] classification of heart failure, left ventricular stroke volume, N-terminal B-type natriuretic peptide [NT-proBNP] level).

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-

label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

REFERENCES

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3. Sekijima Y. Hereditary Transthyretin Amyloidosis. 2001 Nov 5 [Updated 2024 May 30]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1194/. Accessed April 23, 2025.
4. Maurer MS, Sabahat B, Thibaud D, et al. Expert consensus recommendations for the suspicion and diagnosis of transthyretin cardiac amyloidosis. Circ Heart Fail. 2019;12(9):e006075.
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6. Yadav JD, Othee H, Chan KA, et al. Transthyretin Amyloid Cardiomyopathy-Current and Future Therapies. Ann Pharmacother. 2021;55(12):1502-1514.
7. Fontana M, Berk JL, Gillmore JD, et al. Vutrisiran in Patients with Transthyretin Amyloidosis with Cardiomyopathy. N Engl J Med. 2025;392(1):33-44. doi:10.1056/NEJMoa2409134.

EFFECTIVE DATE

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