



MVP Health Care Medical Policy

Medicare Part B: Transthyretin-Mediated Amyloidosis Therapy

Type of Policy: **Drug Therapy**

Prior Approval Date: **08/01/2024**

Approval Date: **12/01/2025**

Effective Date: **02/01/2026**

Related Policies: **N/A**

Refer to the MVP website for the Medicare Part D formulary for drugs that may be covered under the Part D benefit.

Drugs Requiring Prior Authorization (covered under the medical benefit)

J0222- Onpattro™ (patisiran)

J0225 Amvuttra (vutrisiran)

Overview/Summary of Evidence

Hereditary transthyretin amyloidosis (hATTR) is an inherited disease that often affects the liver, nerves, heart and kidneys. It is characterized by the deposit of an abnormal protein called amyloid in multiple organs of the body where it should not be, which causes disruption of organ tissue structure and function. The amyloid buildup most frequently occurs in the peripheral nervous system, which can result in a loss of sensation, pain, or immobility in the arms, legs, hands and feet.

Indications

Onpattro™ is indicated for the treatment of the polyneuropathy in hereditary transthyretin-mediated amyloidosis in adults. The active substance in Onpattro is a 'small interfering RNA' (siRNA), a very short piece of synthetic genetic material that has been designed to attach to and block the genetic material of the cell responsible for producing transthyretin. This reduces production of defective transthyretin, thereby reducing the formation of amyloids and relieving the symptoms of hATTR amyloidosis.

Amvuttra is indicated for the treatment of the polyneuropathy in hereditary transthyretin-mediated amyloidosis in adults. In March 2025, Amvuttra received a new indication for the treatment of wild type or hereditary transthyretin amyloid cardiomyopathy for the reduction of cardiovascular mortality, cardiovascular-related hospitalization, and urgent heart failure visits. The active substance in Amvuttra is a 'small interfering RNA' (siRNA), a very short piece of synthetic genetic material that has been designed to attach to and block the genetic material of the cell responsible for producing transthyretin. This reduces production of defective transthyretin, thereby reducing the formation of amyloids and relieving the symptoms of hATTR amyloidosis.

Policy Criteria

A. Onpattro will be considered medically necessary for the treatment of the polyneuropathy of hATTR amyloidosis in adults who meet the following criteria:

- Member has documented transthyretin (TTR) mutation as confirmed through genetic testing AND symptomatic polyneuropathy (i.e. weakness, sensory loss, decreased motor strength, decreased gait speed) characterized by ONE of the following:
 - Baseline polyneuropathy disability (PND) score < IIIb (see reference table in Appendix A)
 - Baseline FAP (familial amyloid polyneuropathy) Stage 1 or 2 (see reference table in Appendix A)
- Documentation indicating a 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
- Prescribed by a neurologist, immunologist, geneticist or physician who specializes in the treatment of amyloidosis

Initial approval will be for 6 months

Extension requests will be approved up to 6 months if current documentation indicates disease stability or improvement in symptoms (e.g., decrease in neuropathic pain, improved motor function, quality of life assessment, and/or serum TTR levels)

B. Amvuttra will be considered medically necessary for the treatment of the polyneuropathy of hATTR amyloidosis in adults who have **previously failed or have a contraindication to Onpattro**, AND who meet the following criteria:

- Chart notes documenting a failure or contraindication to OnpattroMember has documented transthyretin (TTR) mutation as confirmed through genetic testing AND symptomatic polyneuropathy (i.e. weakness, sensory loss, decreased motor strength, decreased gait speed) characterized by ONE of the following:
 - Baseline polyneuropathy disability (PND) score < IIIb (see reference table in Appendix A)
 - Baseline FAP (familial amyloid polyneuropathy) Stage 1 or 2 (see reference table in Appendix A)
- Documentation indicating a 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
- Baseline documentation of disease status must be submitted if applicable such as 10-meter walk test, quality of life assessment, nutritional health assessment or modified body mass index (mBMI), and ability to perform activities of daily living
- Prescribed by a neurologist, immunologist, geneticist, cardiologist, or physician who specializes in the treatment of amyloidosis
- **Initial approval** will be for 6 months, continuation requests up to 6 months.
- **Extension requests** will be approved up to 6 months if current documentation indicates disease stability or improvement in symptoms (e.g., decrease in neuropathic pain, improved motor function, improved gait speed, improved quality of life assessment, improved ability to perform activities of daily living, increased mBMI, and/or serum TTR levels

Amvuttra will be considered will be considered medically necessary for the treatment of wild type or hereditary transthyretin amyloid cardiomyopathy for the reduction of cardiovascular mortality, cardiovascular-related hospitalization, and urgent heart failure visits when all the following criteria is met:

- Chart notes documenting a failure or contraindication to self-administered medications for the diagnosis
- Chart notes documenting a diagnosis of wild type or hereditary transthyretin-mediated amyloidosis cardiomyopathy AND baseline disease severity
- Chart notes documenting member has New York Heart Association (NYHA) functional class I to III heart failure.

- Member must not have NYHA class IV disease
- Documentation of the presence of TTR genotype confirmed by genetic testing for hereditary transthyretin-mediated amyloidosis
- 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
- Prescribed by or in consultation with a geneticist, cardiologist or physician specializing in the treatment of amyloidosis

Initial approval will be for 6 months

Extension requests will be approved up to 6 months if current documentation indicates disease stability or improvement in symptoms (e.g., quality of life assessment, decrease cardiac related hospitalizations)

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Appendix A:

Polyneuropathy Disability Score (PND) Reference Table

- Stage 0: No impairment
- Stage I: Sensory disturbances but preserved walking capability
- Stage II: Impaired walking capability but ability to walk without a stick or crutches
- Stage IIIa: Walking only with the help of one stick or crutch
- Stage IIIb: Walking with the help of two sticks or crutches
- Stage IV: Confined to a wheelchair or bedridden

Familial Amyloid Polyneuropathy (FAP) Stage Reference Table

- Stage 0: No symptoms of sensory or motor neuropathy
- Stage 1: Unimpaired ambulation; mostly mild sensory, autonomic, or motor neuropathy in lower limbs
- Stage 2: Requires assistance with ambulation; mostly moderate impairment progression in lower limbs, upper limbs, and trunk
- Stage 3: Confined to wheelchair or bedridden; severe sensory, autonomic, and motor involvement of all limbs

Exclusions

- Age, dose, frequency of dosing, and/or duration of therapy outside of FDA approved package labeling
- Concurrent use of Tegsedi with Amvuttra, Onpattro, or tafamidis
- Concurrent use of Vyndaqel and Vyndamax
- Treatment with Onpattro for members without the presence of a polyneuropathy symptoms associated with hATTR amyloidosis
- Treatment with Onpattro when member has form of amyloidosis that is not due to a genetic mutation in the TTR gene

References

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