



MVP Health Care Medical Policy

Medicare Part B: Transthyretin-Mediated Amyloidosis Therapy

Type of Policy: Drug Therapy
Prior Approval Date: N/A
Approval Date: 11/01/2023
Effective Date: 01/01/2024
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.

Drug(s) Requiring Prior Authorization (covered under the medical benefit)

J0222- Onpattro™ (patisiran), injection 0.1 mg

J3490 Amvuttra (vutrisiran), 25mg/0.5mL prefilled syringe for injection

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. 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.

TegsedTM is indicated for treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults. TegsedTM is an 'antisense oligonucleotide', 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 transthyretin, and the formation of amyloids, relieving the symptoms of hATTR amyloidosis.

Vyndaqel and Vyndamax are indicated for the treatment of wild type or hereditary transthyretin amyloid cardiomyopathy in adults to reduce cardiovascular mortality and cardiovascular-related hospitalization. Wild type amyloidosis does not involve genetic mutation- wild type occurs usually in older population when the normal TTR protein becomes unstable and begins to form amyloid fibrils. Hereditary amyloidosis is an inherited mutation in the DNA making the TTR protein unstable and form amyloid fibrils. It works as a selective transthyretin (TTR) stabilizer. Transthyretin amyloid cardiomyopathy is caused by the accumulations of transthyretin amyloid fibrils, which consist of TTR monomers. Tafamidis works by binding to sites on TTR and slowing monomer dissociation. Please note that Vyndaqel and Vyndamax are not equivalents on a mg-per-mg basis.

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:

- 18 years of age or older
- Patient has documented transthyretin (TTR) mutation as confirmed through genetic testing AND Presence of polyneuropathy characterized by ONE of the following:
 - Baseline polyneuropathy disability (PND) score < IIIb (see reference table)
 - Baseline FAP (familial amyloid polyneuropathy) Stage 1 or 2.
- 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

- Patient has clinical signs and symptoms of polyneuropathy (i.e. weakness, sensory loss, decreased motor strength, decreased gait speed)
- Prescribed by a neurologist, immunologist, or physician who specializes in the treatment of amyloidosis

Initial approval will be for 6 months, continuation requests up to 6 months.

Continuation of therapy will be considered medically necessary with documentation of 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:

- 18 years of age or older
- Patient has documented transthyretin (TTR) mutation as confirmed through genetic testing AND Presence of polyneuropathy characterized by ONE of the following:
 - Baseline polyneuropathy disability (PND) score < IIIb (see reference table)
 - Baseline FAP (familial amyloid polyneuropathy) Stage 1 or 2.
- 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
- Patient has clinical signs and symptoms of polyneuropathy (i.e. weakness, sensory loss, decreased motor strength, decreased gait speed)
- 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, or physician who specializes in the treatment of amyloidosis
- Serum vitamin A levels must be monitored and/or patient is monitored by an ophthalmologist

Initial approval will be for 6 months, continuation requests up to 6 months.

- Continuation of therapy will be considered medically necessary with documentation of 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)

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**

Exclusions

- Dosing, age, and/or frequency outside of the FDA approved package labeling
- Concurrent use of Onpattro and Tegsedi is considered experimental and investigational. The safety and effectiveness of this combination has not been established.
- Treatment with Onpattro for individuals without the presence of a polyneuropathy symptoms associated with hATTR amyloidosis.
- Treatment with Onpattro when patient has form of amyloidosis that is not due to a genetic mutation in the TTR gene

References

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