MVP Health Care Medical Policy

Medicare Part B:
Transthyretin-Mediated Amyloidosis Therapy

Type of Policy:	**Drug Therapy**
Prior Approval Date:	**11/01/2023**
Approval Date:	**08/01/2024**
Effective Date:	**10/01/2024**
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

J0225 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.

Tegsedi™ is indicated for treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults. Tegsedi™ 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:

- 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)
    - Baseline FAP (familial amyloid polyneuropathy) Stage 1 or 2 (see reference table)
- 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, 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:

- 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)
    - Baseline FAP (familial amyloid polyneuropathy) Stage 1 or 2 (see reference table)
- 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, 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, 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

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 with Tegsedi
- 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

1. ONPATTRO (patisiran) [package insert]. Cambridge, MA: Alnylam Pharmaceuticals, Inc; 2018.
2. Coutinho P, Martins da Silva A, Lopes Lima J, Resende Barbosa A. (1980) Forty years of experience with type I amyloid neuropathy. Review of 483 cases. In: Glenner G., Costa P., de Freitas A., editors. (eds), Amyloid and Amyloidosis. Amsterdam: Execerpta Medica, pp. 88–98

3. Yamamoto S, Wilczek H, Nowak G, et al. Liver transplantation for familial amyloidotic polyneuropathy (FAP): a single-center experience over 16 years. Am J Transplant. 2007 Nov;7(11):2597-604.
4. Adams D, Suhr OB, Dyck PJ, et al. Trial design and rationale for APOLLO, a Phase 3, placebo-controlled study of patisiran in patients with hereditary ATTR amyloidosis with polyneuropathy. BMC Neurol. 2017 Sep 11;17(1):181.
5. Adams D, Gonzalez-Duarte A, O'Riordan WD, et al. Patisiran, an RNAi Therapeutic, for Hereditary Transthyretin Amyloidosis. N Engl J Med. 2018 Jul 5;379(1):11-21
6. Alnylam Pharmaceuticals. The Study of an Investigational Drug, Patisiran (ALN-TTR02), for the Treatment of Transthyretin (TTR)-Mediated Amyloidosis in Patients Who Have Already Been Treated With ALN-TTR02 (Patisiran). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2018 April 12]. Available from: https://clinicaltrials.gov/ct2/show/NCT02510261. NLM Identifier: NCT02510261.
7. Institute for Clinical and Economic Review: Draft Evidence Report - Inotersen and Patisiran for Hereditary Transthyretin Amyloidosis: Effectiveness and Value. July 20, 2018.
8. Tegsedi Prescribing Information. Boston, MA: Akcea Therapeutics, Inc.; October 2018.
9. Benson MD, Waddington-Cruz M, Berk JL, et al. Inotersen treatment for patients wth hereditary transthyretin amyloidosis. N Engl J Med 2018;379:22-31. DOI: 10.1056/NEJMoa1716793.
10. Tafamidis. Clinical Pharmacology [Internet]. Tampa (FL): Elsevier. c2021- [cited 2021 June 25]. Available from: http://www.clinicalpharmacology.com
11. Amvuttra Prescribing Information. Cambridge, MA: Alnylam Pharmaceuticals, Inc; June 2022.
12. Vultrisiran. Clinical Pharmacology [Internet]. Tampa (FL): Elsevier. c2022- [cited 2022 June 17]. Available from: http://www.clinicalpharmacology.com
13. ONPATTRO (patisiran) [handout/package insert]. Cambridge, MA: Alnylam Pharmaceuticals, Inc; 1/2023.
14. Amvuttra Prescribing Information. Cambridge, MA: Alnylam Pharmaceuticals, Inc; 2/2023
15. Tegsedi Prescribing Information. Watham, MA: Akcea Therapeutics, Inc.; 5/2021.
16. Vyndaqel and Vyndamax Prescribing Information. New York, NY: Division of Pfizer, Inc.; 10/2023